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JUVENILE NASOPHARYNGEAL ANGIOFIBROMA.

A Theory of Pathogenesis.*†‡

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HISTORICAL.

Historically, juvenile angiofibroma was probably included in the early descriptions of nasal polyps, as described by Hippocrates[1] in the Fourth Century, B.C., and by the Eighteenth Century was recognized by the individual characterization distinguishing hard, fibrous polyps from soft, mucous polyps. Probably the earliest description of this tumor, which "commonly occurs in persons about the time of puberty," was by Chelius[2] in 1847. Much was written in the early Nineteenth Century describing the various facial deformities caused by large nasal polyps, and the operations to remove these bulky tumors. The sex selectivity of the angiofibroma was practically unobserved except for a few isolated clinicians such as Legouest,[3] who in 1865 noted the predilection for these tumors in males, and Gosselin[4] who in 1876 observed the tendency for spontaneous regression after sexual maturity. About the same time (1878) Bensch,[5] in Germany, published the first comprehensive report on this nasal tumor; however,

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Chaveau[6] in 1906 was the first to suggest the term "juvenile angiofibroma."

The surgical removal of these tumors was attempted as early as the Second Century, A.D., by the cultured Roman physician, Celsus, who in his compendium to surgery described removal by digital or wire snare, and tearing off of tumors with forceps. Hot iron cautery and injection of escharotics were attempted in later centuries. Langenbeck[7] in 1834, advocated one of the first definitive approaches to the nose and nasopharynx. Modifications of this are still used at the present time. In the latter part of the Nineteenth Century, tracheotomies and ligation of both external carotid arteries were mentioned as preliminary steps before the definitive sanguineous nasopharyngeal surgery. Senn published a volume in 1900, quoting the works of Ollier and Rogue,[8] wherein descriptions of different approaches to the nasopharynx were presented. Some of these have been recently rediscovered.

HISTOGENESIS AND THEORIES OF ORIGIN.

The most widely accepted theory of origin of the nasopharyngeal fibroma is that the tumor is derived from embryologic chondrocartilage during the development of the cranial bones. The basiocciput is joined to the body of the sphenoid by embryonal cartilage. The ossification of this cartilage occurs in the second decade of life. It is from the perichondrium lining this and other postnasal spaces, according to Bensch and Ewing,[9] from which this tumor is thought to originate. New and Kirch[10] do not agree with this viewpoint, since it does not explain the position and location of the tumor on that basis. They quoted Coener's theory of the tumor being one of bone in which the chondrocranium would be the matrix of the tumor. In this way, the various positions, the character, and the spontaneous involution could be better explained.

Figi and Davis[11] suggested that acute inflammation and trauma may be exciting or accelerating factors. Martin, Ehrlich, and Abels[12] in their excellent presentation of this subject were unable to find any systemic disease as a causative factor.

Infection, nasal allergy, heredity, trauma, or ethnic origin did not appear to be etiologic factors. Their only observation was that over half of the cases appeared to have underdevelopment of secondary sex characteristics. In the review of the subject by Hughes,[13] it was thought that anatomic, craniopharyngeal duct inclusion might be a factor in the etiology of this tumor.

Spielberg[14] suggested that chronic suppurative posterior sinusitis may be a contributing factor in the etiology of juvenile nasopharyngeal angiofibroma, and made a plea for better examination in sinusitis with polyps. Som and Neffson[15] believed that there is an inequality of the development of the bones of the skull so that the periosteum is unable to produce typical bone; and, with increased endocrine growth stimulus during puberty, hypertrophy occurs in place of bone formation. They suggested that spontaneous regression occurs when ossification is complete. This regression has been proposed by others, such as Persky[16] and Milligan,[17] to occur because, with the closure of suture lines by ossification, the growth stimulus and blood supply to the tumor are diminished.

THEORY OF PATHOGENESIS.

Since Koch's postulates are not applicable in tumors and since the nasopharyngeal fibroma has never been successfully induced in an animal experimentally, it is necessary to evolve a theory, or *modus operandi*, when dealing with this mesenchymal tumor. This theory is predicated upon inductive and deductive types of reasoning based on previous experimental data applied and interpreted by the author in the light of clinical experience and microscopic study of four cases of juvenile nasopharyngeal fibroma. It is believed that this tumor is due to an alteration in the pituitary androgen-estrogen axis, most probably involving overactivity of the pituitary and reflecting itself in a ground substance response to a vascular tumor. This conclusion is reached after a careful study of the literature and the author's cases, with microscopic evidence to show the response of the tumor before and after treatment.

An attempt will be made to satisfy the following obvious

characteristics of the tumor which in previous explanations and theories have led to highly controversial opinions:

1. The fibrous nature of this tumor.
2. The angiomatous component of this tumor.
3. The sex predilection for males.
4. Its exclusive location in the nasopharynx.

1. FIBROUS NATURE OF THE TUMOR.

a. Connective Tissue Component.

In discussing the fibrous nature of this tumor, it is necessary to discuss the connective tissue and ground substance of the body in general. In 1933, Klinge[18] conceived that the connective tissue of the body could respond as an organ to disease. Klemperer[19] classified a large number of conditions as diseases of connective tissue. Until then, the extracellular compartment was not considered as an organ either in morphology or function; however, with the advent of a unified concept of collagen disease, and especially since the study of Cortisone, we have begun to consider the ground substance as an organ. The anatomy of this *milieu interieur*, as Claude Bernard described this space, is composed of cells—mainly fibroblasts, mast cells, lymphocytes, plasma cells, and undifferentiated mesenchymal cells. The connective tissue fibers are collagen, elastica, and reticulin, of which the first is the most important in our thesis. The other important component for this discussion is the amorphous ground substance, consisting of mucopolysaccharides and glycoproteins in varying degrees of polymerization. Ordinarily it has a gel-like consistency and is not very water-soluble; however, under certain abnormal conditions, it may become depolymerized, more fluid and finally, water-soluble.

The physiology of the extracellular compartment may be altered by many conditions. This is important, since this space represents the internal environment of the cells and, therefore, many of the protective reactions and defense mechanisms aimed at maintaining the homeostasis of the cell, occur in this area. The effect of infection (such as gangrene

and streptococci) has been known to spread through tissues with great rapidity. Duran-Reynals[20] pioneered in showing that this spreading factor was due to hyaluronidase acting on the hyaluronates of the ground substance. Some poisonous snakes and insects excrete a spreading factor of a similar nature, which explains the rapid spread of tumefaction following their injection or bite.

Certain neoplasms also have the ability to increase the amount of ground substance and fibrous reaction to a given tumor. Antihyaluronidase has been found in animals and human subjects bearing these tumors. This desmoplastic diathesis or fibrous tissue reaction to tumors has been magnificently presented by Pack and Ariel[21] in their study on this subject.

Metabolically, the tissues of the extracellular compartment have no blood supply of their own and they must depend upon chemicals, usually enzymes, as proper food for maintenance and growth; thus, deficiencies of Vitamin C, an anaerobic oxidative substance, markedly reduces the ability for healing and fibroblastic proliferation. Pyridoxine deficiencies cause increase in the metachromasia of the ground substance. Hypoproteinemia causes an osmotic change in the ground substance which also retards wound healing.

The spreading factor of the enzyme hyaluronidase is inhibited by many of our commonly used medications, such as epinephrine, morphine, antihistamine, salycilates, and rutin. It is probable that at least part of the beneficial effect of the therapy to the patient is on this basis.

The hormonal effects on connective tissue have been observed empirically for many years. Their relationship to the more intimate details of ground substance reaction was more extensively discussed at the Fifth Connective Tissue Conference in 1954.[22] In brief, the following hormonal effects are noted and are intimately related to the author's thesis: Estrogen decreases the permeability of the ground substances; gonadotropic hormones increase its permeability; desoxycorticosterone enhances the deposition of collagen and fibroblastic proliferation; and the excretion of testosterone and estradiol

inhibits these reactions. The sex skin of the monkeys demonstrated the changes of the ground substances under the normal hormonal cyclic control.[20,21,23,24]

The preceding and following observations on endocrine connective tissue responses are being assembled and presented to substantiate the author's contention that there are ample experimental data to explain the microscopically-observed connective tissue alterations in response to estrogen therapy (see Figs. 1, 2, 3, 4). Geschickter and Lewis[25] reported several interesting observations on tumors of these tissues. They also agreed that the basal fibroma probably originates from the periosteum of the chondrocranium in the region of the basiocciput. They were able to induce an increase in the maturity and amount of connective tissue in the breast and uterus of monkeys by the injection of estrin. They were also able to produce similar changes with anterior pituitary gonadotropic hormone only if the gonads were present.

This author has commented to the pathologist on several occasions on the similarity between young keloid and angiofibroma. This was more extensively studied[25] when hormone assays were made of a huge keloid of the ear. In this case, the bio-assay of the keloid revealed 13,000 rat units of gonadotropic hormone and 3,500 rat units of estrin. The keloid, like other desmoid tumors related to sex, may become arrested or regress when the hormone state is altered. The conclusion of these investigators[25] is worth noting: "The results would seem to indicate that tumors of connective tissues have the power to hold or concentrate both anterior pituitary gonadotropic and estrogenic substances. These hormones are not merely stored in the tissue, but also have a direct influence on the growth of the tissue where they are found, as confirmed by experimentation."

In general, the connective tissue makeup is essentially similar, being mucopolysaccharide and glycoprotein in nature. Histochemically, it is made up of protein fibers of several specific types embedded in a mucous ground substance. The protein fibers are of three main types: *1.* elastica; *2.* collagen, and *3.* reticulin. The mucopolysaccharides have been more extensively investigated and the histochemical characteristics

better studied. It is impossible within the scope of any single work to cover the tremendous amount of basic and voluminous investigations which have been accumulated in the past 15 years, particularly since the studies of the action of corticosteroids. Discussion will be limited to those facts which are pertinent to this thesis. Persson,[26] in discussing the multiple functions of the ground substance, postulated that it is an end organ for many hormones, including adrenocortical, sex, and thyroid. Figs. 1 and 2 would seem to substantiate this contention.

In studying the distribution of mucopolysaccharides by chemical methods in connective tissue, five were identified:[27]

1. Hyaluronic acid.
2. Chondroitin sulfate A.
3. Chondroitin sulfate B.
4. Chondroitin sulfate C.
5. Hyaluronosulfate.

It appears that the quantitative difference of each of these components, together with the degree of polymerization, determines to a great extent what the mesenchymal tissue is to be. Whether it will be vitreous humor, synovial fluid, hyaline cartilage, aorta, or skin can be demonstrated histochemically. It would suggest from the various studies on connective tissue makeup that, depending upon the character and type of stimulus, the chemical nature would be altered, and one of these forms might be changed into another. There is ample evidence to indicate that this might occur. Upon study, it would appear that the case reported by Wirth and Shimkin[28] actually could have started out as a juvenile angiofibroma and become a chondrosarcoma, despite the fact that this might be an extremely rare occurrence. Cartilage has been shown to develop from the periosteum of membrane bone by Pasternack, Lillie and Jones,[29] and extraskeletally by Binkley and Stewart.[30] The latter authors, in their excellent discussion, have stressed the concept of metaplasia of connective tissue into bone under some unknown influence. They also believed that one of the conditions for ossification and calcification is

a circulatory one caused by: *a.* hyaline obliteration of capillaries; *b.* development of cavernous vessels favoring stasis and probable anoxemia or hypoxia. This latter condition probably exists in a juvenile angiofibroma since measurements have never been actually made of blood flow rates through the tumor. Despite the fact that clinically, when cut, it bleeds so frightfully, stasis still may be present. This bleeding is believed to be due to the large number of transsected, small vascular spaces whose cross sectional sum total would equal the size of almost any vessel in the body with the exception of the aorta; also, the lack of a muscular coat about these vessels prevents them from closing off. Pressman,[31] in a series of photomicrographs of the aorta grafted on to the trachea, showed that the cartilage was eventually replaced by bone from changes in its connective tissue stroma. This appeared to be due to ischemia or stasis changes and could be reproduced regularly in the animals. Clinically, the juvenile angiofibroma always appears to have considerable congestion. The degree of chronic congestion may be another factor which determines the variable density of the collagen found in this tumor. It seems obvious that in some manner the vascular component must exert a profound influence on the connective tissue component.

The source of the mucopolysaccharides, which make up the ground substance, has been highly controversial and exciting.

1. For many years it was assumed that the fibroblast itself was the direct source of connective tissue.

2. Asboe-Hasen[32] found a correlation between the number of mast cells and the quantity of hyaluronic acid in tissues. The presence of numerous mast cells can be seen, particularly in a toluidine blue stained photomicrograph. As seen in Figs. 5, 6, 7, 8, 9, and 10, the metachromasia is dependent upon high polymer hyaluronic acid and the pink-violet is considerably depleted when treated with the enzyme hyaluronidase. This enzyme may be of streptococcal source (which is more specific for hyaluronic acid), or it may be from the testicular source which is more diversified in its depolymerization of mucopolysaccharides. The latter type (Wydase) was selected because of the ease of availability. Schiff's periodic acid

stain is nonspecific and stains a large group of substances including glycogens, polysaccharides, glycoproteins, and many others. Its stain depends upon the free aldehyde group so that when treated all polymers, both large and small, are stained with this dye substance (see Figs. 11, 12, 13, 14, 15, 16). The colloidal iron stain shows the blue staining ground substance which is also depolymerized by hyaluronidase incubation (see Figs. 17, 18, 19, 20, 21, 22). All histochemical microscopic slides used in this thesis were made by the controlled simultaneous preparation method of Weisskopf and Burn,[33] so that as far as possible, changes in the staining characteristics are histochemical, not artifacts.

3. Connective tissue may be formed by the action of the primitive fibroblasts on the substrate of the ground substance. Histochemical data suggest that this cell is especially related to the fibrous elements of the connective tissue while the mast cells, which also make heparin, reflect or produce changes in the ground substance.

4. Recently, Curran[34] published his findings which show that the capillary endothelium has the capacity to elaborate mucopolysaccharides. Activity of this function of the endothelium is increased in tissue repair, tumor stroma, and osteogenesis. It synthesizes sulfated mucopolysaccharides and is concerned functionally with anticoagulation, transfer of nutrients from the blood, and the making of new ground substance.

b. Connective Tissue Stain.

The significance of the histochemical changes observed in the study of these various staining techniques is still controversial; however, one has only to look at the amount of information obtained from the routine hemotoxylin and eosin stain to see that many substances are either not stained at all or fail to show any contrast in the components of their supporting structure. The Schiff stain (PAS) demonstrates this well in the intense pink perivascular staining about young blood vessels. This might give some support to the work of Curran[34] showing the intimate relationship between the endothelium and the production of mucopolysaccharides.

The colloidal iron stain depends upon the affinity of the mucopolysaccharides for colloidal iron and is demonstrated as an intense blue coloring, particularly about the blood vessels. The collagen has a red-brown color. A study of sections with this stain certainly indicates the abundance of material never shown to exist in routine H & E stains.

The toluidine blue stain demonstrates mucopolysaccharides in the ground substance and the large number of mast cells. This would be in keeping with the observations of Asboe-Hansen[22,32] as to the function and contribution of the mast cells to connective tissue.

All of the above histochemical studies for ground substance are influenced by the presence of hyaluronidase. This enzyme breaks the bonds in the large polymers of hyaluronic acid. The result is a depolymerization and loss of staining characteristic in the toluidine blue and colloidal iron preparations. Since PAS depends upon the aldehyde linkage, the effect of hyaluronidase is minimal in that it only breaks the large polymers into smaller ones which still have an available aldehyde group when stained. This is observed in the slight change in staining characteristic following treatment of the tissue with hyaluronidase.

A more complete discussion and further references on the technical aspects of the stains are presented by Weiskopf and Burn.[33]

The question arises: Is this a major source of ground substance, and to what extent is it controlled by the endocrine system of the body? The problems to be solved about basic studies of the ground substance and connective tissues of the body are innumerable; but with each added fact, enlightenment becomes greater, and the knowledge regarding juvenile angiofibroma is augmented since it is intimately related to progress in this field of investigation.

2. ANGIOMATOUS COMPONENT OF THE TUMOR.

It is difficult to separate the fibrous from the vascular nature of this tumor, but perhaps better understanding of its character can be obtained if an attempt is made to analyze

each component separately. While studying the endocrine aspect of the vascular component, it becomes apparent that much of this work was done on atrophic rhinitis. Since many of the aspects of this condition are in the diametrically opposite end of the fibrovascular spectrum and, therefore, are produced by a dysfunction of the pituitary endocrine action opposite to that theorized to exist in juvenile nasopharyngeal angiofibroma, a simultaneous study of both of these conditions can be productive.

Soskin and Bernheimer,[35] while studying and observing the mechanism of estrogenic effect on the nasal mucosa in atrophic rhinitis, noted a specific proliferative effect of estrin. This produced a secondary hyperemia which they concluded was due to the acetylcholine-like action of estrin. Reynolds[36] and Fagin and Reynolds,[37] in their studies on the effect of estrin on the animal uterus, observed vascular alteration. In general, they measured a considerable decrease in the number of vessels per square millimeter in the treated over the untreated uterus. These observations are confirmed by the findings shown of the estrogenic effect on juvenile angiofibroma as demonstrated in Figs. 3 and 4. Mortimer, Wight, and Collip[38] made a significant contribution in their excellent paper dealing with atrophic rhinitis. They performed cranial skiagrams or X-rays in 68 cases of ozena. A large majority showed a dyspituitary state during or subsequent to the growth period. Speculation on the mode by which a dyspituitary constitution might influence the morphologically specialized conchal mucosa, led these investigators to study the nasogenital relationship of monkeys. They recognized the fact that the administration of estrogenic substances produced a specific response in the turbinate mucosa similar to that resulting in other sex skin areas. They concluded that atrophic rhinitis may be genetically transmitted in special familial constitutions in which anterior pituitary lobe function is unstable in secretory activity, nature, or time of activity. A very important piece of work corroborating the influence of sex hormones on the vascular system was written by Edwards, et al.,[39] on their studies of cutaneous vascular and pigmentary changes in castrate eunuchoid men. The observed cutaneous areas showed large venous beds with dilated capillaries. This condition

could be reversed by giving the castrate testosterone propionate. The excitability of the cutaneous blood vessels could be increased by the use of estradiol and decreased by testosterone. This study is particularly interesting when one reflects on the observations of Martin, Ehrlich, and Abels[12] discussing the underdevelopment of secondary sex characteristics in over one-half of their case reports concerning angiofibromas. The discussion about the action of estrogen and androgen on the blood vessels of the body is by no means entirely a nebulous theoretical concept. Koch, Escher, and Lewis[40] used estrogenic hormone in treating hereditary hemorrhagic telangiectasis of the nose in five cases, with excellent results. Fortunately, they were able to measure the urinary gonadotropin and follicle-stimulating hormone, and found these values to be high. Conversely, the measurement of the estrogen level, made simultaneously during the period of hemorrhage, was low. Treatment with ethinyl estradiol resulted in the suppression of the pituitary, and within one week an actual change in the mucous membrane was observed. The color became pink, and the crust and edema of the membrane disappeared. In the three females and two males on whom this treatment was employed, the telangiectasia decreased and disappeared in some of the patients. The disappearance of the edema strongly suggests a change in the ground substance as well, and marked involution of the blood vessels suggests the pituitary suppression and local estrogen activity, much in the same manner as is being hypothecated by the author in juvenile angiofibroma. In general, it is the purpose, therefore, to present in this section the accumulated data to confirm and support the contention that the various hormonal components have a specific effect upon the blood vessels of the body, each having its own characteristic response. The mechanism for these specific responses is not entirely understood as yet.

3. SEX PREDILECTION FOR MALES.

The reason for the predilection of this tumor for the male seems to be for the most part, almost self-explanatory in the light of the findings noted in the previous section on the endocrine nature of its angiomatous component. In brief, the human body contains both estrogenic and androgenic sub-

stances. In the preadolescent male, as he commences to enter adolescence, there is a hypoandrogenic state with its characteristic basal vascular bed. The pituitary may be normally active, or relatively hyperactive in that the threshold for gonadal response or balance may be so altered that growth stimulus continues despite the lag in the production of androgen. This growth stimulus from the pituitary under certain conditions has the capacity to produce fibrous tumors. This is best demonstrated in acromegaly, the extreme of pituitary somatotropic hypersecretion. The incidence of tumors in these cases is much higher than normal, most of them being fibromas of the skin. Here all mesenchymal tissues are stimulated to grow, which accounts for the thick coarse skin of the acromegalic who has a tendency to form keloids both with and without trauma. The basic effect in these cases is in the ground substance which is plentiful and shows intense metachromasia and numerous mast cells and fibroblasts. The bundles of collagen fibers are thick and coarse. These findings have been frequently noted by Asboe-Hansen,[41,43] who has contributed monumentally to the knowledge of connective tissue in health and disease.

The present method for measuring slight subclinical deficiencies or overactivity of any part of the endocrine system is crude at best. Only when profound pathologic changes are found is it possible to give the disease a name and measure the gross disturbance of secretions. Precise blood values for the male and female sex hormones of the normal individual have yet to be determined.

Whenever the feature of sexual dimorphism occurs in any disease entity, it provokes considerable speculation as to its cause. Recently, Rauch[43] noted the hormonal dysfunction in those cases of laryngeal carcinoma developing in women and classified them in groups. One series showed slight androgenous hair distribution, atrophic breasts, deepening voice changes, and vascular anomalies of the terminal vessels. Here, again, this observation of the effects of sex hormones on tumors and blood vessels was noted. He presented a highly involved neuro-endocrine basis for the development of these tumors. Despite its complexity, his interesting thesis

appears to be in the right direction to permit greater understanding of basic pathologic processes of tumor formation. It is apparent that if estrogens have the ability to inhibit hypervascularity, in contrast to peripheral vasodilatation caused by its acetylcholine effect, and can also decrease the permeability of the ground substance, then, juvenile angiofibromas, by their very nature of genesis, would be discouraged in the female. This is an obvious clinical truism. Upon this basis, since the tumor does not exist in the female (except very rarely), if we could convert a patient with this tumor into a female type it might cause the tumor to involute. These speculations have borne fruit, at least in the limited number of cases tried in the present series.

4. EXCLUSIVE LOCATION IN THE NASOPHARYNX.

The exclusive location of this tumor in the nasopharynx requires an evaluation of what factors or what tissues function in the nose particularly, but not generally in the rest of the body. That the nose is a sexual organ has been recognized for many centuries as far back as Hippocrates and Celsus. One has only to think phylogenetically of the function of the nose in all other mammals to realize that it is *via* this organ that most animals find their mates and their food. At that level of life, the nose is necessary for survival and procreation. The observed alteration of the nasal mucosa during menstruation is generally credited to Bresgen[44] in 1881, who noted and studied this phenomenon. The further endocrine implications were studied clinically in relationship to pregnancies, sexual excitement, as well as menstruation, by such early writers as MacKenzie,[45] Endriss,[46] and Fliess.[47] In 1912, Sieffert[48] integrated much of the previous data, and recently Mohun[49] brought these data up to date and concluded that the change in the nose depended to a large extent on the ovarian hormones in women. Mortimer, Wright, and Collip,[50] in their outstanding study of the endocrine effect on the nasal mucosa of monkeys, clearly showed the nasogenital relationship. In these animals, if the turbinates were excised, the testes did not descend. This response was most profound when the middle and inferior turbinates were removed. The nasal mucosa reacts to estrone synchronously with a change of

nipple and sex skin. The response of the turbinate in the intact, endocrinely balanced, normal animal is specific, showing redness and swelling. This specific response can be produced with estrone in a castrate female but it cannot be produced in the similarly prepared castrate animal by using pituitary gonadotropin. This would indicate that a local effect was necessary. The recognition of the local effect suggested its use by these investigators[50] for atrophic rhinitis. Pseudopregnancy in rats has been induced by the application of silver nitrate to the nasal mucosa, by Rosen and Shelesnyal.[51] This, again, emphasizes the nasogenital relationship since nasal stimulation is able to elicit an ovarian response and diestral prolongation.

After reading the above findings, one might be tempted to ask how it is possible that estrogens produce one effect in one patient or animal and a different effect in another. To communicate this explanation, one may revert to a dynamic German philosophic term, "the *Gestalt*." This is a configurational pattern for that moment which is under a constant change with every change of data. Thus, the configuration of the total endocrine pattern in any one patient is almost totally unknown except for the measured amount administered or which may be measured by the present available gross methods. The further proof that this incomplete knowledge is recognized is that the laboratory values are practically never at a set figure but instead, a range for the "normal"; therefore, each individual response in the disease state depends to a great extent on the *Gestalt* and on the myriad of unknowns influencing the *milieur interieur* as well as the general environment. This should explain to some extent the diversity of responses to any endocrine therapy and serve to stimulate efforts to decrease the myriad of unknown factors.

Since the vascular makeup of the inferior turbinate is hormonally sensitive, it does not seem difficult to conceive that in the developmental stage of the nasopharynx a small nidus of similar vascular tissue might have been caught up in the large sheet of mesenchyma developing into the periosteum. The basiocciput, the basisphenoid, and ethmoid are all of similar chondrocranial origin. We have many other parallels

to this ectopic location of tissue in embryology, particularly of the same germ layer. That the angiomatous component might be the most important has been suggested by Martin, Ehrlich, and Abels.[12] The fibrous response is probably desmoplastic in nature, provoked by the local ectopic vascular tumor and the general endocrine response to it of the ground substance of the body. It is well nigh impossible to prove the speculation that these tumors arise as responses to ectopic vascular tissue, since no one has ever reported the observation of a juvenile angiofibroma developing from its incipiency. Usually when first seen, they are already of moderate size. Nonetheless, it seems logical that here we have sex-hormone-sensitive vascular tissue in the inferior turbinate, and as long as this tissue is in its proper location, the body response is normal, not desmoplastic. If, however, a small portion of vascular tissue of the inferior turbinate type were to be found in the periosteum in the developmental stage, there would be adequate reason for the mesenchyma of the periosteal layer to provoke an attempt to wall off this ectopic tumor with connective tissue, its only potential for response. The response would not begin until the sensitizing hormones start to circulate in puberty.

CLINICAL COURSE.

The juvenile angiofibroma is a benign expanding entity, often somewhat encapsulated and noninfiltrating, which originates in the posterior nares or nasopharynx. It is composed of mixed angiomatous and fibrous tissues occurring almost solely in adolescent males, with a tendency to involute spontaneously upon full sexual maturity.

The phrase, "tendency to spontaneous involution," as used in contrast to the general comment in the literature, is based upon the author's personal experience with four cases of active, young, healthy males—all in the second decade of life. This is supported by the more voluminous experience of Figi and Davis[11] in which they stated, "We never observe the complete spontaneous disappearance of these fibromas that is often referred to in the literature."

In the outstanding report by Martin, Ehrlich and Abels,[12]

PRESENTATION OF JUVENILE ANGIO-FIBROMA WITH PHOTOGRAPHS OF THE NASOPHARYNX

M. SCHIFF, CAPTAIN MC, USN

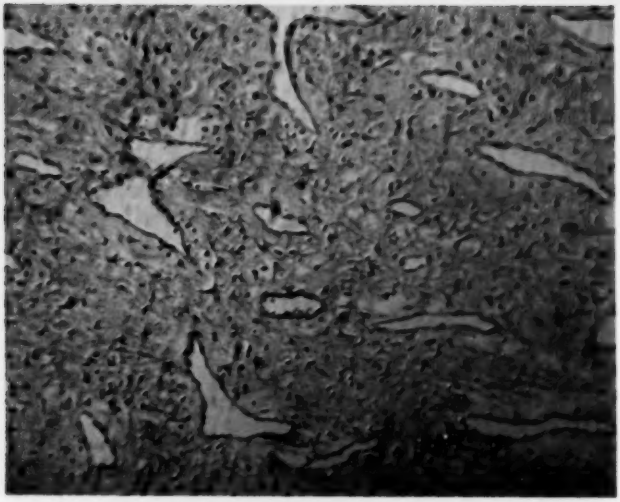


Figure 1.—Case 4. Pre-estrogen therapy photomicrograph. Hematoxylin and eosin stain of the angio-fibroma shows many young and older endothelial lined spaces with a thin immature type of connective tissue stroma. (X 180)

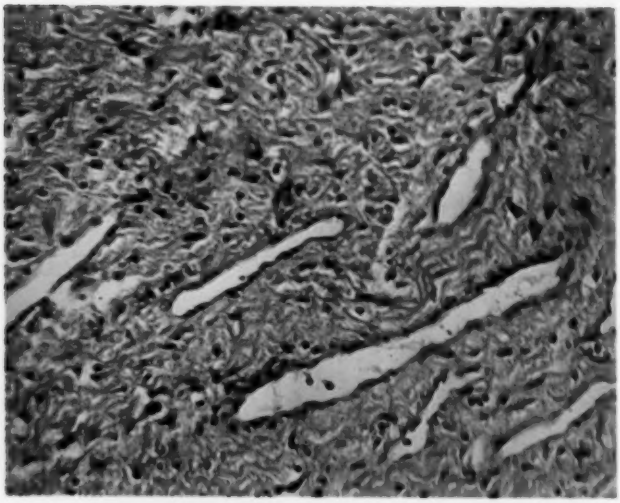


Figure 2.—Case 4. Post-estrogen therapy photomicrograph. Hematoxylin and eosin stain of the angio-fibroma shows marked maturing of the connective tissue stroma with thick strands of collagen. The blood vessels show a decrease in number but an increase in size and maturity. (X 180)

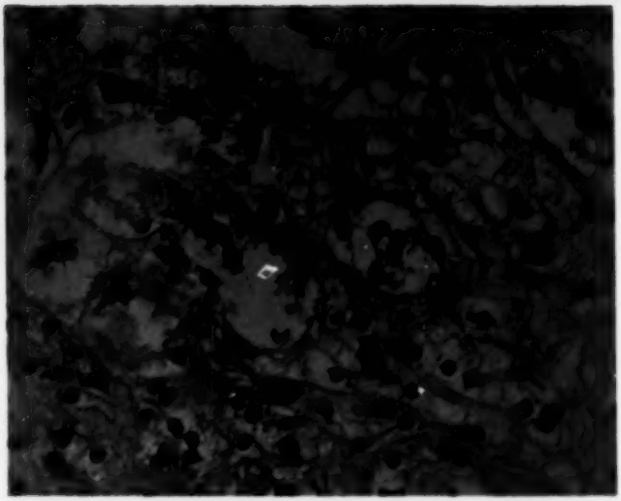


Figure 3.—Case 4. Pretreatment hematoxylin and and eosin stain photomicrograph to emphasize the thin areolar like quality of the supporting connective tissue seen in Figure 1. (X 400)

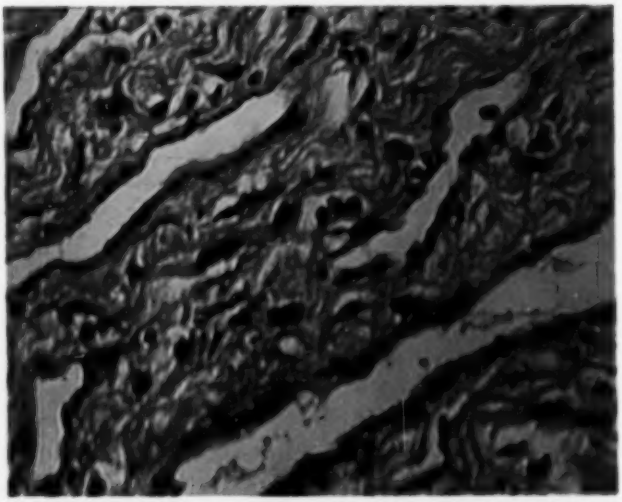


Figure 4.—Case 4. Post-treatment photomicrograph. Hematoxylin and eosin stain shows the denseness and maturity of the connective tissue and the large vascular spaces in Figure 2. (X 400)

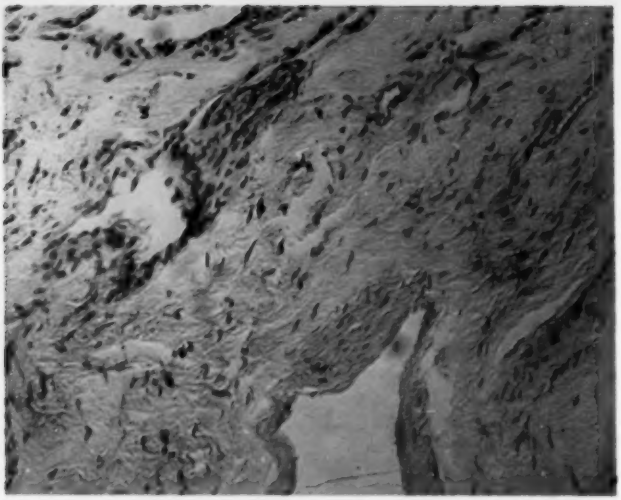


Figure 5.—Case 1. Toluidine blue stain shows the pink-violet metachromasia of the perivascular ground substance with numerous mast cells in this photomicrograph. (X 180)

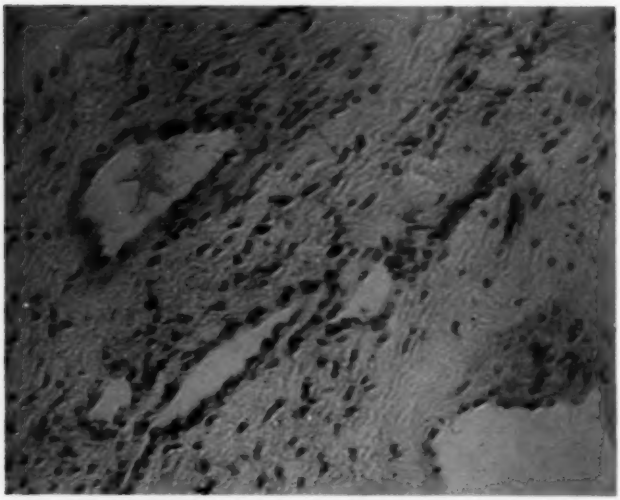


Figure 6.—Case 1. Photomicrograph. Toluidine blue stain treated with 750 T.R.U. Wydase. The loss of metachromatic stain of the large polymer mucopolysaccharides is noted. Mast cells are still clearly visible. (X 180)

Figure 7.—Case 2. Photomicrograph. Toluidine blue stain shows the pink-violet metachromasia of the ground substance together with many mast cells. (X 180)

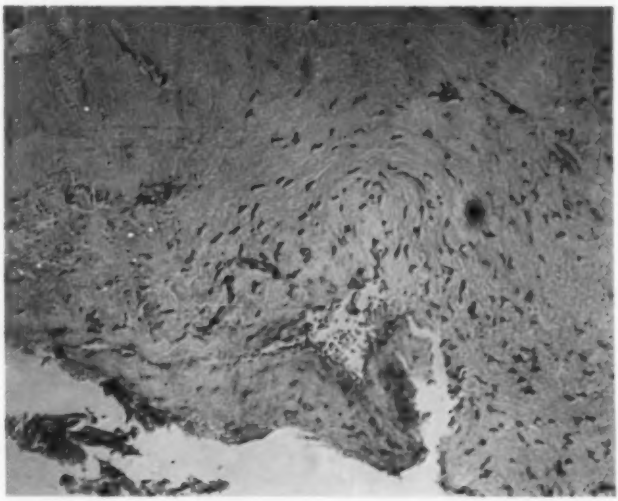


Figure 8.—Case 2. Photomicrograph. Toluidine blue stain following incubation with 750 T.R.U. Wydase. There is almost a complete loss of the metachromasis following depolymerization. Mast cells still are visible. (X 180)

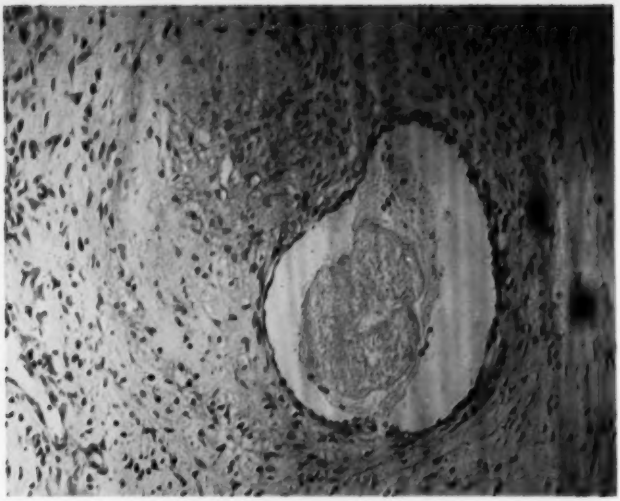


Figure 9.—Case 3. Photomicrograph. Toluidine blue stain shows pink-violet metachromatic material about the vessel. Mast cells well visualized. (X 180)

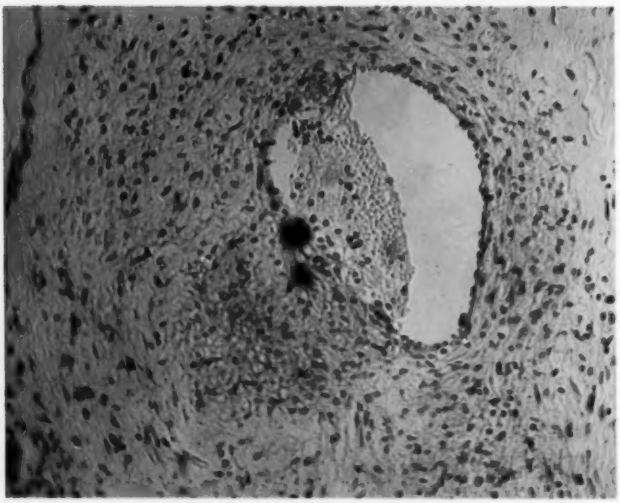


Figure 10.—Case 3. Photomicrograph. Toluidine blue stain following incubation with 750 T.R.U. Wydase. Shows a considerable decrease in the metachromasis but mast cells still present. (X 180)

Figure 11.—Case 1. Photomicrograph. Schiff periodic acid stain shows the general diffuse pink coloring of the perivascular mucopolysaccharides. (X 180)

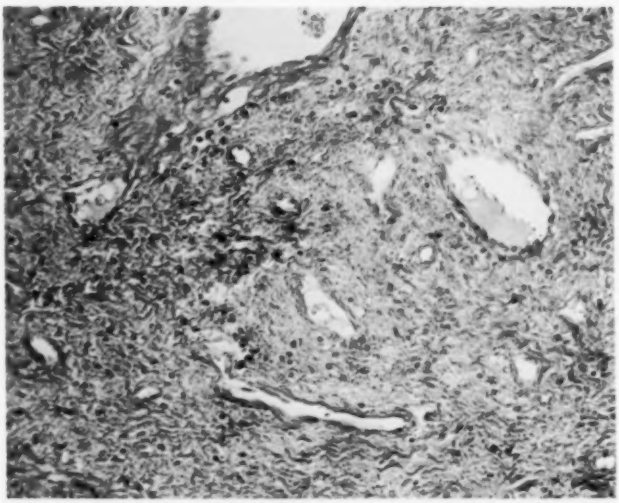


Figure 12.—Case 1. Photomicrograph. Schiff periodic acid stain with 750 T.R.U. Wydase. Shows a decrease in the amount of perivascular pink coloring. The nonspecific nature of the stain can be noted when compared with the untreated tissue. (X 180)

Figure 13.—Case 2. Photomicrograph. Schiff periodic acid stain shows its nonspecific nature. Collagen stains orange, and perivascular mucopolysaccharides are bright pink. (X 180)

Figure 14.—Case 2. Photomicrograph. Schiff periodic acid stain following incubation with 750 T.R.U. Wydase. Minimal changes noted as stain is non-specific for the size of the polymer. (X 180)

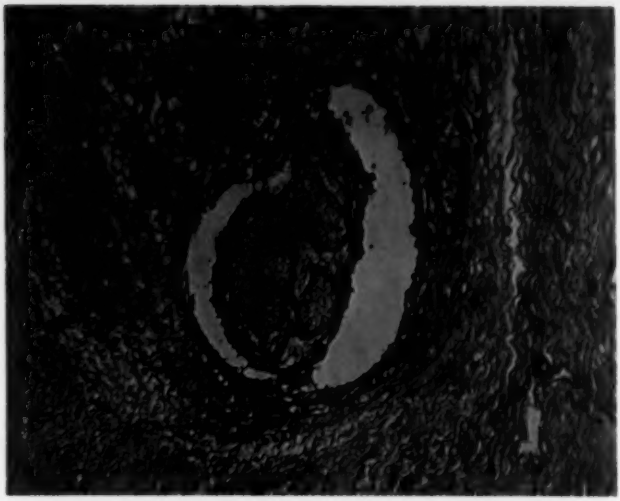


Figure 15.—Case 3. Photomicrograph. Schiff periodic acid stain shows the perivascular pink staining ground substance. Collagen stains orange. (X 180)

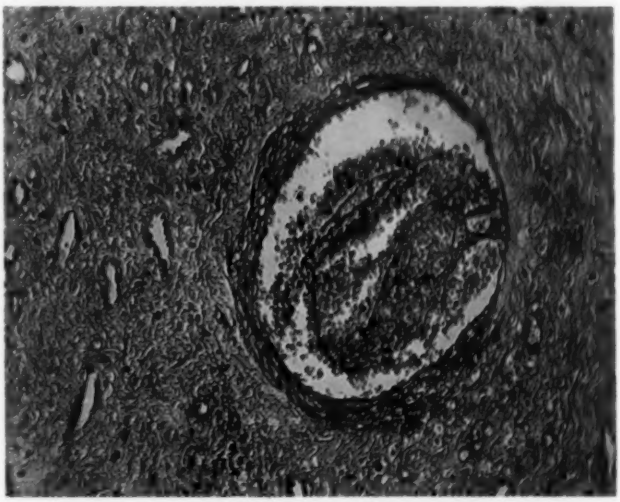


Figure 16.—Case 3. Photomicrograph. Schiff periodic acid stain following incubation with 750 T.R.U. Wydase. Stain is not remarkably different than untreated section. There is a decrease in the perivascular stain. (X 180)

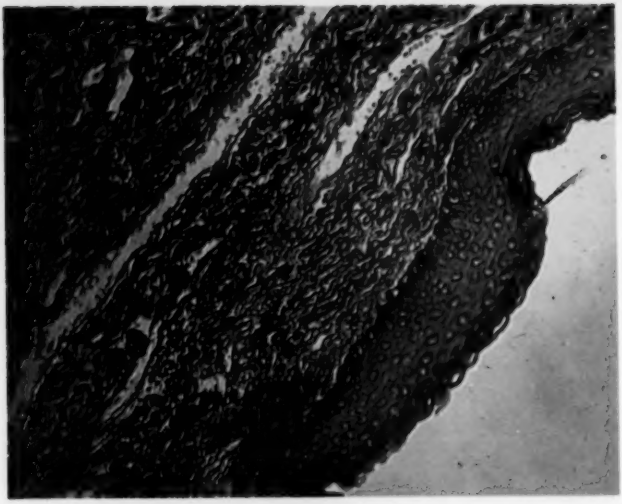


Figure 17.—Case 1. Photomicrograph. Colloidal iron stain shows blue stain of mucopolysaccharides in and about the blood vessels. Mature Collagen stains red. (X 180)

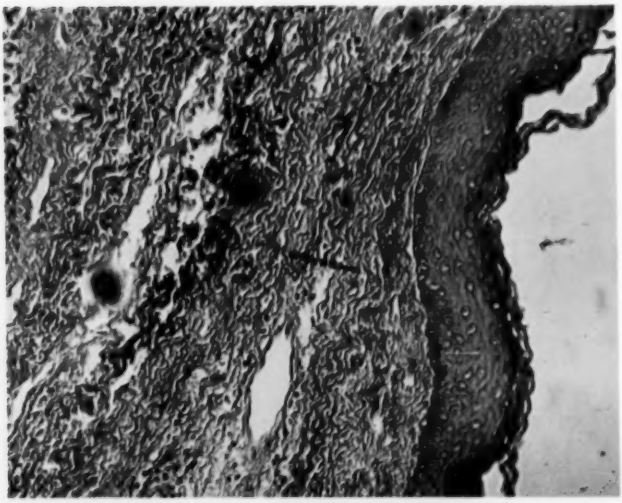


Figure 18.—Case 1. Photomicrograph. Colloidal iron stain following incubation with 750 T.R.U. Wydase. Minimal change in appearance of collagen, only slight decrease in perivascular ground substance. (X 180)

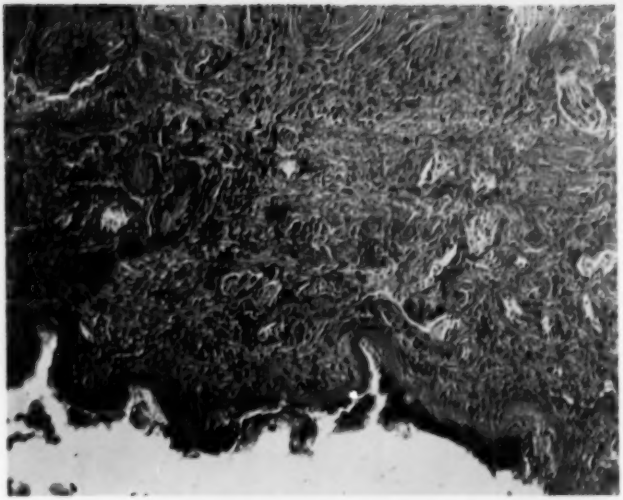


Figure 19.—Case 2. Colloidal iron stains show the unusual well marked basement membrane and the diffuse amount of mucopolysaccharides and mucoprotein. (X 180)

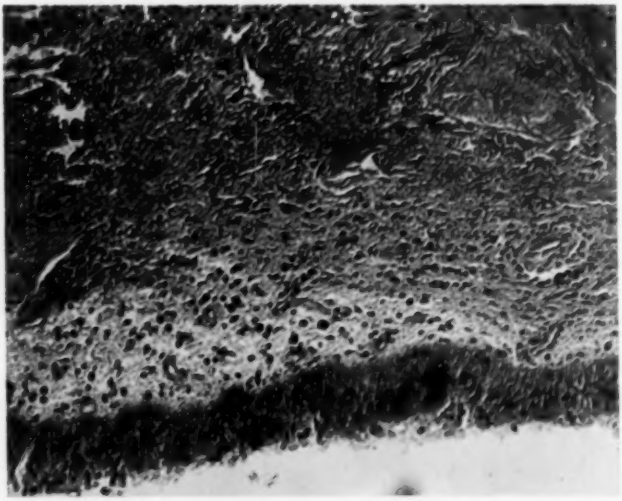


Figure 20.—Case 2. Colloidal iron stain following incubation with 750 T.R.U. Wydase. Marked depolymerization of the basement membrane and mucopolysaccharides are noted. (X 180)

Figure 21.—Case 2. Colloidal iron stain shows the abundance of blue staining ground substance particularly about the new vessel formations. (X 180)

Figure 22.—Case 3. Colloidal iron stain following incubation with 750 T.R.U. Wydase. There is a considerable loss in the metachromasia. However, mast cells are still fairly visible. (X 180)

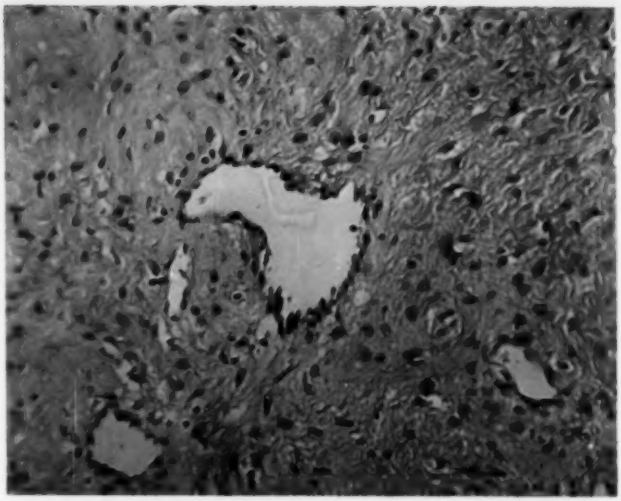


Figure 23.—Case 1. Postoperative photomicrograph. Hematoxylin and eosin stain of the angiofibroma shows tumor containing vascular spaces with prominant and mature endothelial cells. They are surrounded by fibrous connective tissue with some fibtoblasts visible. There is no evidence of thrombosis of the vascular spaces, necrosis, or other changes attributable to radiation effect. (X 180)

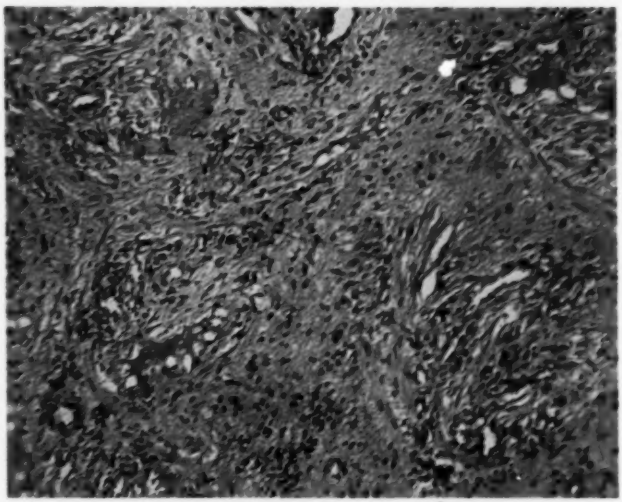


Figure 24.—Case 2. Photomicrograph. Hematoxylin and eosin stain of angiofibroma shows some round cell infiltration together with areas of young and also mature vascular spaces. Connective tissue shows various degrees of maturation. (X 180)

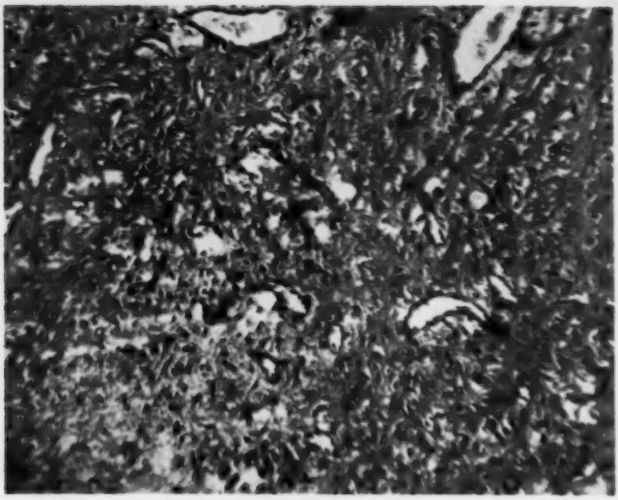
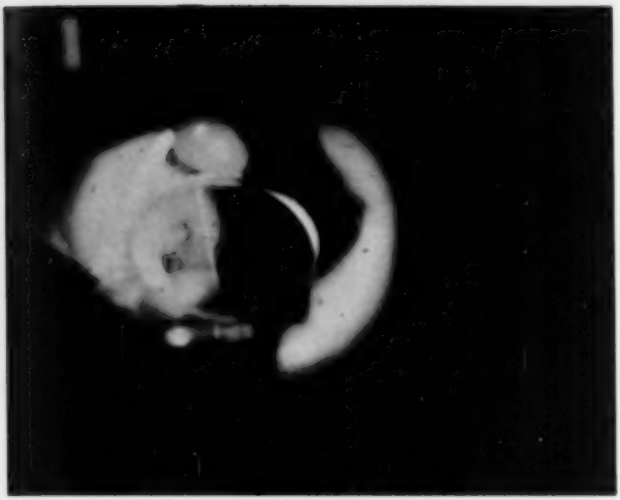


Figure 25.—Case 3. Photomicrograph. Hematoxylin and eosin stain of angiofibroma shows many connective tissue strands many of which are fibroblasts. Blood vessels are seen in various stages of development. (X 180)

Slide 1.—Case 1. Preoperative nasopharyngeal colored slide shows the round red mass in the right nasopharynx with white exudate on its surface.



Slide 2.—Case 1. Postoperative appearance of nasopharynx shows right eustachian tube and choana with no evidence of tumor within visible limits.

Slide 3.—Case 2. Preoperative nasopharyngeal colored slide shows a large lobular mass in the nasopharynx, mostly on the left.

Slide 4.—Case 2. Postoperative nasopharyngeal colored slide shows the absence of the tumor with the left posterior naris and choana visible.

Slide 5. (Not Shown) *Case 3.* Preoperative nasopharyngeal colored slide shows a large mass in the nasopharynx, predominently on the left.

Slide 6. (Not Shown) *Case 3.* Preoperative, post-estrogen, colored slide of nasopharynx shows a change in color and size of the tumor mass.

Slide 7. (Not Shown) *Case 3.* Postoperative colored slide shows a spacious nasopharynx but a recurrence visible in the center of the mirror.

Slide 8.—Case 4. Preoperative, pre-estrogen nasopharyngeal colored slide shows a smooth red tumor mass on the right with some visibility of the left choana.

Slide 9. (Not Shown) *Case 4.* Preoperative, post-estrogen therapy, nasopharyngeal colored slide shows the degree of the recession of the tumor, 36 days after treatment, to the extent of being able to see the right eustachian tube and part of the right choana superiorly.

Slide 10.—Case 4. Postoperative nasopharyngeal colored slide shows absence of the tumor and the clear visibility in the mirror of the right eustachian tube and the posterior tips of the middle and inferior turbinates.

which analyzed 29 cases of this tumor during a 20-year period, it was reported that none of these occurred in the female. In contrast to this, the excellent comprehensive and analytic study by Figi and Davis[11] of 144 cases, reported over a 30-year period was divided into two groups: the first group of 63 cases, reported between 1910-1939, included five females, or 7.9 per cent; in 51 cases reported from 1940-1949, all were males, or 0 per cent females; with an overall average of 4.4 per cent females for the entire series. It is of considerable interest to speculate on the reason for the large statistical divergence between the first and second group of their series.

The onset of symptoms varies from seven to 19 years, with an average of 14 years in one report,[12] and ten to 21 years of age, with an average of 18 years for the second series.[11] It is estimated that the incidence of this tumor is .05 per cent of all neoplasms of the head and neck. The signs and symptoms of this entity have a general march of progression and almost invariably occur in the following order: Nasal obstruction; recurrent epistaxis; progressive deformity of the palate, face, and throat; rhinolalia, and anosmia; not infrequently, however, alarming epistaxis may be the first complaint. The march of symptoms is usually brought to an abrupt halt by the thorough and astute observations of the first clinician to examine the patient. This fact becomes more impressive when it is realized that symptoms in one series were present from one month to six years with an average of one and one-half years. Because of the extreme vascularity of the tumor, heroic measures are often required to control bleeding. These may be from tamponade to bilateral carotid ligation. The general clinical course of the disease is such that constant observation is necessary, and the proper selection of both time and method for definitive treatment is of utmost importance.

DIFFERENTIAL DIAGNOSIS.

It is extremely important to make a differential diagnosis between the angiofibroma and any of the other tumors which occur in the nasopharynx. The general characteristic of this tumor is a smooth, occasionally lobular, firm, hard, red mass

with occasional areas of ulceration and exudation, depending upon the amount of bleeding, trauma, or secondary infection which has been present previously. These characteristics differ greatly from nasopharyngeal carcinoma, and the differential diagnosis for this entity is not difficult. The chordoma in this area might well produce some confusion, but roentgenographic diagnostic studies should be of considerable help.

Adenoid tissue may cause nasal obstruction but is easily differentiated by the characteristic, soft, irregular mass along the mucosa.

Benign tumors of the salivary gland in the nasopharynx may be firm like an angiofibroma, but their appearance and location should make the diagnosis apparent. Chondrosarcoma or angiosarcoma can produce a considerable amount of confusion. This has been noted in detail in the case report by Wirth and Shimkin.[28] Even tissue obtained by biopsy in the early stage of the disease failed to reveal the true nature of the tumor. The diagnosis was later confirmed at secondary and tertiary surgical procedures, and also at necropsy when metastatic areas were found in the lung fields. The appearance of pulmonary metastases would immediately mitigate against a diagnosis of angiofibroma; however, the most common tumor for which a differential diagnosis must be made is the choanal polyp. In general, this is not difficult, for the choanal polyp has its characteristic smooth, glistening surface and a pale, edematous, translucent appearance. There is usually very little definite redness to the tumor, and occasionally a few dilated vessels may be seen on the surface. One of the most important and yet often neglected part of an examination for nasopharyngeal tumor is the digital palpation. The difference in the feeling of a choanal polyp to the finger and that of an angiofibroma is so contrasting that seldom will one be led astray. If the index of suspicion for this vascular tumor remains high, the accidental removal of a misdiagnosed polyp, with its subsequent massive hemorrhage, would be avoided.

CASE REPORTS.

Case 1. E.G.R., Jr., a 20-year-old, well developed, well nourished, brown-

haired, white male, was admitted to the first hospital on Jan. 23, 1950, with the complaint of difficulty in breathing through the right nostril and recurrent epistaxis for the previous nine months. On Jan. 26, removal of the red, firm tumor mass from the right nasopharynx was attempted but not completed due to excessive bleeding; however, the specimen was reported as juvenile angiofibroma. On Feb. 3, a large tumor mass was removed from the nasopharynx with electrocautery, but the excision was not considered complete. Profuse bleeding occurred during the operation and for the following two weeks. He received 1600 *r* of X-radiation in an attempt to scarify the tumor and prevent further bleeding. This was followed by an acute respiratory infection and otitis media, which responded to penicillin therapy. On April 19 he was discharged from the hospital with a moderate sized mass still present in the right choana. On Aug. 31 he was admitted to a second hospital because of recurrent epistaxis and difficulty in breathing. On Sept. 22 he was transferred to this hospital for definitive treatment.

On physical examination a firm, pale red mass was seen in the nasopharynx and after detailed study appeared to be attached to the medial plate of the right pterygoid and the base of the sphenoid across the midline (see Slide 1). The remainder of the physical examination was essentially normal except for hypertrophy of the tonsils.

Laboratory studies revealed a normal hemogram with 7500 white blood cells, 14 gm. hemoglobin, and a platelet count of 213,000. The Kahn test was negative; urine, normal; bleeding and clotting time, normal.

X-ray examination revealed a mass about 3 cm. in diameter lying in the nasopharynx on the right. No osseous destruction was noted. Diffuse clouding of the right antrum and ethmoids was also noted. After a discussion at the Tumor Board, it was suggested that additional X-ray therapy be tried and 1800 *r* at the skin was delivered *via* two alternating portals of 300 *r* daily for a total depth dose of 2970 *r*. This did not seem to arrest the growth of the tumor, and since the patient had had surgery and two courses of X-ray therapy, a consultation was arranged with Hayes Martin, M.D., who suggested testosterone but believed that surgery would eventually be necessary. This proved to be the case. The patient was given 25 mg. of testosterone propionate, q.i.d., for 36 days. The tumor did not appear to grow, but neither was there much evidence of involution. On Jan. 24, 1951, the right external carotid was ligated, the right middle turbinate removed, and the entire mass evulsed with a cold snare of especially heavy piano wire. When this snare was firmly in place through the nose, a cut was made on the prevertebral fascia via the mouth and extended to the periosteum of the sphenoid—not disturbing the tumor. This permitted a plane of cleavage, along which the evulsion could take place. With a pull of tremendous force, the tumor tore free from the nasopharynx taking with it the anterior wall of the right sphenoid with its sphenopalatine artery. The bleeding that followed was brisk but quickly controlled when a few small remaining pieces of tumor were removed (see Fig. 23). A postnasal pack was used to control the slight postoperative bleeding. The nose was unpacked and bleeding was minimal until Feb. 3, when the patient suddenly began to bleed profusely. This was rapidly controlled by fulgurating the area of the evulsed sphenopalatine artery. From this time on, healing was uneventful and the nasopharynx appeared clear except for a small, suspicious, granular mass in the right fossa of Rosenmueller. A biopsy was taken and found to be granulation tissue. All other check biopsies from this area were negative. The patient has had no recurrence (see Slide 2).

Case 2. D.R., a 53-year-old, auburn-haired, well developed, well nourished, white male first noticed difficulty in breathing at age 18, while

in school. At age 20 he had an operation for a deviated nasal septum, after which his breathing was not improved. In March, 1951, he was operated upon for adhesions in the nasal airway to relieve the increasing nasal obstruction. The tumor was first discovered at that time. On March 26, an attempt was made to remove the nasal tumor, but only half of it was excised. The blood loss was about 600 cc. The patient was transferred on June 6 to this hospital for definitive treatment.

On admission the physical examination proved to be essentially negative except for a red, firm mass, 2x2.5x3 cm., attached to the left lateral nasal wall and medial pterygoid plate, obstructing the entire left choana (see Slide 3). A small subdigastric node was palpable on the left. Pubic hair distribution was of gynecoid type. Genitalia were slightly underdeveloped for his age.

Laboratory studies revealed essentially normal urinalysis and hemogram. The white blood cell count was 6800; hemoglobin, 14 gm.

Chest X-ray was normal. X-ray of the skull showed a mass in the nasopharynx measuring 2.5x3x3.5 cm. The anterior, medial, and inferior margins appeared to be free but seemed to merge into the bony structures along the superior and lateral margins. There was no evidence of erosion and invasion.

Because of a history of allergies, appropriate tests were performed showing a 3+ reaction to chicken, nuts, green peppers, malt, and house dust. The patient was given 25 mg of testosterone propionate, q.i.d., for two months, with no dramatic change; however, the growth did not seem to have increased, and slight involution was suggested.

On July 11, under pentothal anesthesia with endotracheal cuff, the left middle and inferior turbinates were removed and the tumor mass well visualized. An attempt was made to remove the tumor with the cautery snare; but only a portion was excised and massive bleeding ensued. This was controlled by a packing. With biting forceps, working *via* the nose and mouth combined, the mucosa was stripped off the prevertebral fascia and the periosteum elevated off the base of the sphenoid. With considerable force this was evulsed, taking with it almost the entire tumor and part of the anterior wall of the sphenoid. The bleeding that followed again was brisk and vigorous but as in other procedures when cleaned down to bare bone, it was easily controlled. About 1500 cc. of blood loss was replaced during surgery. Firm anterior and posterior packs were inserted, and the patient was returned to the ward in good condition. The pathologic report was "juvenile angiofibroma" (see Fig. 24).

On the fifth postoperative day, the last of the packs was removed and brisk, bright red bleeding began. This was easily controlled by precise suction cautery to the antero-superior wall of the sphenoid and the nasopharynx repacked. On July 19, eight days after surgery, the patient complained of headache, was listless, lethargic, and developed a swelling of the left cheek. His fever rose to 104.2° F. A repeat complete physical examination at that time failed to show any neurologic or systemic cause for this marked elevation. It was assumed that this probably represented a thrombosis in the pterygomaxillary space. The patient was placed on a regimen of aspirin and forced fluids in addition to the systemic penicillin and aureomycin he had already been given. The following day 3 to 4 ft. of vaseline packing was removed and the bleeding was controlled by cautery. No repacking was necessary. On July 21 the patient had improved considerably and the edema of the left side of the face had subsided to a large extent. Continuous inspection of the nasopharynx revealed only a small nubbin of tissue on the lateral wall. This was eventually removed and the pathologic report was "pyogenic granuloma." The nasopharynx was cleaned of crust by saline irrigation. No

evidence of recurrence was noted at any time and the patient was discharged on Dec. 7, 1951 (see Slide 4).

Case 3. W.E., a 23-year-old, well developed, well nourished, married, white male with carrot-red hair, was admitted to the first hospital on Sept. 12, 1951, and transferred to this hospital three days later for definitive treatment. His chief complaint was recurrent nosebleed and progressive difficulty in breathing on the left. He had a history of severe nasal hemorrhage dating from age 18 in the last year of high school. These were treated, but no one looked in his nasopharynx until admission to this hospital.

The physical examination was essentially normal except for a large mass, 2.5x2x2.75 cm., filling the entire left choana and extending down into the area of the prevertebral fascia on the left (see Slide 5). The mass appeared to be attached to the posterior and lateral wall of the left nasopharynx. The patient had freckles, red hair, and a gynecoid distribution of pubic hair. Genitalia were normal.

Laboratory studies showed normal urinalysis and hemogram.

X-ray examination demonstrated well developed sinuses. The frontal sinuses were somewhat larger than normal, as often seen in pituitary over-activity. The mass was observed in the left nasopharynx, but no erosion or invasion was visualized.

It was decided to try estrogen therapy in this case since androgen therapy produced some change but not adequate involution. The patient was given 5 mg. of estrogen (Stilbesterol) three times daily for one month. During this time, he noted enlargement of the breast and a decrease in libido. This, having been explained to the patient and his wife beforehand, did not disturb the family relationship. During the period of estrogen therapy, there was a very definite change in appearance of the tumor from a large, red, swollen, firm mass, to one that was considerably smaller and which had become pale purple in color, suggesting that of an allergic mucosa (see Slide 6). The tumor had become almost stony hard to palpation.

It had been previously decided to remove the tumor regardless of the response to hormonal therapy. On Jan. 16, 1952, under pentothal endotracheal anesthesia with a cuff, the left inferior turbinate was removed; the tumor was grasped with a heavy piano wire snare, and an attempt was made to evulse it as had been done in previous cases. The greater portion of the tumor came free from the anterior wall of the sphenoid (see Fig. 25); however, there appeared to be some residuum on the medial pterygoid plate and some small areas of involvement of the prevertebral tissue down to the C-1. This was removed with a cutting cautery loop. Blood loss was moderate and brisk but apparently considerably less than in the previously treated cases. One thousand cubic centimeters of blood was replaced while in the operating room. This was more than adequate.

The postoperative course was uneventful except for the removal of the last of the packs on the fifth day, resulting in a brisk, severe hemorrhage which was controlled by packing and extensive cautery. Five hundred centimeters of blood was again replaced.

On Feb. 25, a check biopsy from the left lateral wall of the nasopharynx revealed residual tumor. This area was extensively fulgerized on April 12. The patient remained asymtomatic until May 8, 1953, when he returned with some swelling on the left cheek. Re-examination revealed a small nub of tissue of the lateral wall of the nasopharynx posteriorly (see Slide 7). Biopsy of this tissue revealed juvenile angiofibroma. Lateral X-rays of the skull and sinuses demonstrated a probable involvement of

the left pterygomaxillary space. He was given a course of X-ray therapy through two portals for a total of 2600 *r* tissue dose. This was supplemented by radon seeding of 6 mc. of the pterygomaxillary space *via* a Caldwell-Luc approach. The posterior wall of the left antrum during surgery appeared to be paper-thin, with a highly vascular tumor beneath its periosteum. A series of radon seeds was geometrically inserted so as to increase the tissue dose to a total of about 3700 *r*. On June 4, the swelling appeared to have decreased almost entirely, and no tumor was visible. The patient was discharged from the hospital with the tumor apparently under control. In October, 1955, the author was notified by letter of the recurrence of the tumor, and in the early part of 1956 an extensive exenteration of the left pterygomaxillary space was performed.

Case 4. L.P., a 20-year-old, well developed, well nourished, white male, with carrot-red hair, was admitted to this hospital on March 20, 1952, with the chief complaint of progressive difficulty in breathing through the right side of the nose. No history of epistaxis was present. Nasal obstruction started about one year prior to admission. Being the fourth case of this tumor seen within a period of two years, the preoperative diagnosis was made immediately.

The physical examination was essentially normal except for a red, firm tumor, 1.5x2x3 cm., seen in the nasopharynx, mostly on the right and free on all surfaces except for its attachment to the anterior wall of the right sphenoid and right medial pterygoid plate (see Slide 8). The hair distribution was essentially normal. Genitalia were smaller than usual for the patient's age.

Laboratory examinations showed normal hemograms and urinalysis.

X-ray examinations demonstrated a 2x2x3 cm. mass in the right nasopharynx. Some clouding of the right ethmoid was also noted.

Because of previous experience in endocrine therapy, it was decided to take a biopsy specimen of the tumor prior to instituting estrogen therapy to see whether the clinical evidence was confirmed by microscopic proof of changes in the nature of this tumor. On May 20, three pieces of tissue were removed from different sections of the tumor (see Fig. 1). This was to insure proper sampling. The bleeding was brisk and bright red, with each bite, but it was readily controlled by suction cautery.

Following this, a course of estrogen therapy, (Stilbesterol) 5 mg. three times daily for a month, was given. Enlargement and discomfort of the breasts were noted, together with a loss of libido. At the end of therapy, the patient noted increased ability to breathe and smell through the right side of the nose, a pleasure he had not been able to enjoy for some time. The change in the clinical and microscopic appearance of the tumor can only be described as dramatic (see Figs. 1 and 2). The condensation of the collagen and maturity of the diminished number of blood vessels of these representative sections indicate the manner in which estrogen affects both the ground substance and vascular component (see Figs. 3 and 4). Clinically, the tumor changed from a large, red, firm mass, with a somewhat boggy mucosal covering, to a mass which decreased about one-half in size and increased in firmness to feel almost like cartilage. Kodachrome studies of the pre- and postoperative state could not show all the changes because of technical difficulties (see Slide 9). The patient was able to blow air through the right nostril—a function which was impossible prior to therapy.

It had been decided prior to estrogen therapy that this tumor would be removed surgically regardless of the hormone response. On Aug. 11, under pentothal endotracheal anesthesia, a large piano wire snare was placed about the mass after having removed the right inferior turbinate.

A cut was made through the periosteum of the sphenoid and elevated below the attachment of the tumor. This gave a plane of cleavage for the evulsion of the tumor on this occasion. Considerable force was required to tear the tumor free, and it came out with a good margin of normal mucosa. The time required for its removal was very short by comparison, and the blood loss was estimated at only 250 cc. Some difficulty was encountered in getting this mass of tissue out through the right naris since its macroscopic measurement on removal was 3x4x1.3 cm. The nasopharynx, being packed off, the mass was manipulated from its entrapment in the right external nasal vestibule. On gross sectioning of the specimen, several cystic-looking spaces were noted, one having a transverse diameter of 0.6 cm. The tumor appeared to have been removed in its entirety at this time (see Slide 10).

The postoperative course was uneventful, with no major hemorrhages when the packing was removed. The nasopharynx healed so well that it was difficult to believe the size and source of the original tumor. Follow-up check in 1956 revealed no evidence of recurrence.

It is with considerable regret that, due to conditions beyond our control, histochemical studies of this case were not possible.

TREATMENT.

Treatment for juvenile angiofibroma may be placed in several categories; however, the individual therapy of a given case must be equated and treated as a specific problem of its own. Since this tumor is generally benign, but locally malignant, it should be treated with this in mind. It is felt by many authorities that the mass will involute and present no further problem for the patient. As has been previously noted, the authors with the largest series are in complete disagreement with this feeling. An early decision for treatment will appear to be highly advantageous. Waiting for the expected involution of this tumor is but to wait for the tumor to grow bigger and present more problems at a later date.

Local Chemical Therapy.

The use of local chemical sclerosing agents is a natural thought that occurs when treating tumors which are essentially vascular in nature. McFarland[52] used the following chemicals: two per cent phenol, lithium salicylate, snake venom, and sodium morrhuate. His conclusion was that none of these altered the course of the tumor, favorably or adversely. Sclerosing injections were also used by Figi and Davis[11] in one case. In general, however, injections of this type have little benefit to offer and few present advocates for its use. The injection site bleeds, and if tissue sloughs, there is then a

large, raw, bleeding surface rather than a smooth uninterrupted capsule.

Radium Therapy.

In these highly vascular tumors, the insertion of a trocar for implantation of radon seeds can produce alarming hemorrhage; however, in small recurrences, this modality may afford satisfactory control. The dose and the distance should be so calculated as to produce a maximum sclerosing action with a minimum risk of radionecrosis. Figi[53] and Delavan[54] placed considerable reliance on radium therapy. Four seeds of 1.5 mc. each were placed 1 cm. apart by the author when seeding the left pterygomaxillary space of the patient in Case 3, making a total dosage of 6 mc. as recommended by Martin, Ehrlich, and Abels.[12] The subsequent involution was satisfactory. Forster[55] used two flat applicators of 25 mg. of radium each, with one millimeter lead filter for a period of seven hours. A slight improvement in the area was noted. He then used cautery and additional deep X-ray therapy because of the lateral extension of this tumor. Through the years, radium therapy has had many advocates,[16,56-58] but the consensus is that it is most useful for smaller sized tumors and small recurrences.

X-ray Therapy.

Because the angiomatous elements of many tumors are usually radiosensitive, X-ray therapy is undoubtedly somewhat helpful in reducing the vascularity of this tumor. The obliterative endarteritis of Roentgen-ray therapy will at least slow the growth of new angiomatous tissue and obliterate some of the vascular spaces of the more mature tissue. Probably little, if any effect is noted on the fibrous element. Doses of 1000 to 1500 *r* over each maxilla, or 2000 to 2500 *r* through the hard palate, have been given by Martin, Ehrlich, and Abels.[12]

Since the therapy is given before full facial growth is reached, some flattening of the facial bones from inhibition of their growth centers may occur. This might be minimized by cross-firing of the tumors through several portals, or rotation therapy.

Electrocoagulation.

High frequency or diathermal coagulation has the advantage over the simple hot-wire type of electric coagulation, in that it has penetration in depth. It seems logical to have used this type of therapy since these currents tend to burn deep and seal off blood vessels. The older literature, particularly that from the Continent, has numerous references for the use of electrocoagulation. In 1928 Roure[59] described his treatment of fibroma by this method. The French and Italian literature, particularly, contain numerous references for the use of this method;[60-65] however, in the past 15 or 20 years, the use of high-frequency coagulating current as a prime method of destroying the juvenile angiofibroma has fallen somewhat into disuse. This is in contrast to the frequent use of this modality in the treatment of small recurrences, in which case it is highly effective.

Sex Hormone Therapy.

Boedts[66] from his experience with hormone therapy in the treatment of angiofibroma, described the use of estrone in a case and then followed it with progesterol. When the tumor did not cease its growth, X-ray therapy was then added, and finally the surgical removal of a large part of the tumor was accomplished. This is one of the earliest uses of hormone therapy. Unfortunately, there were no pre- or post-therapy slides which could be considered as demonstrating the effect of the hormone itself on the tumor. The final microscopic section showed considerable X-ray necrosis, together with various degrees of tissue reaction.

Apparently working on the premise that the tumor involutes, the hemorrhagic tendency decreases at maturity, and that it would be desirable to accelerate this maturity, Martin, Ehrlich, and Abels[12] decided to test the use of androgen therapy. Upon the administration of 25 mg. of testosterone propionate, they observed in one case a rapid disappearance of the tumor in the space of one month. In the two cases of the present series observed following androgen therapy, there was some involution, but it was not dramatic. A hypogenitalism syndrome with polycythemia and nasopharyngeal fibroma

was described by Redoglia,[67] indicating the obvious imbalance of the hormonal system in relation to the disease. It is believed that in hormonal dysfunction an attempt should be made to correct this endocrine imbalance. Androgen therapy shows significant histological changes, particularly in the vascular component and the ground substance. Delarue, et al.,[68] noted a decrease in tumor size and a fibrinoid type of degeneration which they believed accounted for the clinical effects of testosterone. The exact nature of this change is not completely discussed in terms of the metachromasia which they described in the ground substance.

Hypogenitalism, which has been noted by many in association with this tumor, is probably due to the overactivity of the anterior pituitary which, in turn, has a suppressive effect on the genital growth. Since the androgen output of the testes is not sufficient to inhibit the pituitary and create a normal balance between the two, a tilt in this axis persists. It is in this type of endocrine configuration that the angiofibroma can potentially develop.

Using a diametrically opposite rationale of endocrine therapy, this author felt that if the angiofibroma were exclusive in the male sex, the alteration of the androgen-estrogen pituitary axis by making the male more female might produce involution of the tumor. Therapy of this type has its well-established parallel in the modern rationale of the treatment for carcinoma of the prostate by castration and high doses of estrogen. Since the therapy appeared to be on a firm logical basis, it was decided to try it on the subsequent two cases. In Case 3, it was used without previous biopsy, as a pilot observation to see whether involution occurred. Dosages of 5 mg. of Stilbesterol for one month, three times daily, were given. The involution was sufficiently exciting to make sure that pretherapy biopsy would be taken in the future. In Case 4, this was done and the involution was even more dramatic. Preoperative microscopic sections (see Fig. 1) show the immature connective tissue and the abundance of young vascular spaces. Post-therapy microscopic sections (see Fig. 2) revealed the maturation of the collagen and a considerable decrease in the number of vascular spaces, together with an

increase in size of the now-existing spaces. Figs. 3 and 4 are high-powered photomicrographs of the pre- and post-treatment findings. Note the marked difference in the tissues; it is hard to believe they are from the same patient. These findings in the human individual confirm and corroborate for the first time the animal and experimental data which have been presented in detail in the preceding sections of this paper. The clinical involution in this case was equally as dramatic (see Slides 8, 9, and 10). It is not meant to suggest that estrogen or any hormonal treatment is the complete answer to the problem for the angiofibroma; however, since it produces maturation in the connective tissue components of the tumor and appears to decrease the amount of bleeding, it is the author's opinion that this type of therapy is certainly worth trying as a supplement to other modalities, particularly prior to surgery.

Surgical Therapy.

There still exists a certain amount of controversy concerning the value of aggressive surgery for this tumor. Martin, Ehrlich, and Abels[12] did not believe that aggressive treatment increased the number of cures; Figi and Davis[11] were of the opinion that it does increase the cure rate. With the acknowledged limited experience in the four cases presented here, it would certainly seem that the earlier the tumors are detected and the smaller they are, the easier would be the possibility of complete removal. In addition, the removal of the periosteum in the nasopharynx to which the tumor is attached definitely facilitates the excision of the tumor and probably results in a higher rate of cure. Again, since these tumors are sometimes treated conservatively[23,69] and do not always cause death when untreated, it is necessary to temper courage with judgment if the tumor mass is of such size that removal would possibly jeopardize life. The surgical removal of these tumors was noted in the historical section of this thesis to start in the Second Century and continue to the Twentieth Century. Due to the fact that a number of approaches are physically limited, there have been cyclic repetitions or rediscoveries of these methods.[70-77] These tumors have been removed transnasally, nasopharyngeally, transpalately, by re-

section of the palate, via a Caldwell-Luc window, with lateral rhinotomy, and an extended Weber-Ferguson type of incision. The approach depends upon the location and extent of the tumor, the skill and dexterity of the surgeon, and other factors which might individualize the treatment of a given patient. The carotid artery may be ligated unilaterally or bilaterally; but some authors feel that because of the nature of the angiofibroma's attachment and its extensive and diverse blood supply, ligation of the external carotid does not decrease the bleeding appreciably. In this series all the tumors were removed by a combined nasal and nasopharyngeal approach, using a heavy piano-wire snare more to hold and for traction than to cut—thereby permitting evulsion of the tumor after the periosteum on the sphenoid is incised and peeled cephalically. Unilateral carotid ligation was performed in one case, which appeared to bleed just as much as those which were not ligated. It is felt that regardless of the degree of involution produced by hormonal or Roentgen therapy, surgical removal is most desirable, if possible.

COMPLICATIONS.

The most obvious complication is bleeding. This may be of a severe nature, either before or after treatment. Postoperative bleeding is not uncommon, particularly if the tumor has been incompletely removed. With the advent of the modern blood bank system, the surgeon has an invaluable ally to help control excessive bleeding. Infection is usually kept under control, particularly with modern antibiotic therapy. Most secondary complications of infections are those incurred because of blockage of the drainage from the sphenoid and ethmoid sinuses. Deformities of the face and palate occur[78] and can be minimized by planned surgical intervention. The intracranial complications of this tumor are serious[79-81] and may occur before or after surgery. Secondary pneumocephalus is, of course, not so serious as the potential meningitis. With the drugs available which have a good passage of the blood brain barrier, control of these infections is easier.

PHOTOGRAPHIC TECHNIQUE.

Since photography of the nasopharynx is a procedure re-

quiring a somewhat difficult technique, it is believed that the experience gained in these cases might be of help to those interested in photographing pathology in this area.

1. Atropine sulphate, 0.4 mg., is injected subcutaneously one-half hour prior to starting photography for the average 18-year-old male.

2. Pharynx and nasopharynx are sprayed with 2 per cent cocaine or 0.5 per cent pontocaine until pharyngeal anesthesia is adequate to prevent or minimize gag reflexes.

3. In order to minimize the amount of contracture of the palatine musculature, with its subsequent closing off of the post-palatal space, 1 per cent xylocaine is injected about the posterior palatine foramen and, if necessary, in the lateral portion of the muculature of the soft palate itself.

The patient is now ready to be photographed. As can be noted by the 35 mm. colored slides, the final pictures are a considerable improvement over the earlier ones. The soft palate is drawn anteriorly and held in position by a self-retaining, multiple-hinged soft palate retractor.*

An extra large special mirror with a 3- to 4-cm. diameter and a somewhat malleable firm handle is placed in the pharynx facing the nasopharynx.

A Kine Exacta camera with extension bellows and a ring electronic flash adapter was used. Any single lens reflex camera which eliminates the parallax problem can be used. The ring strob is a source of light originating about the camera lens to give powerful illumination without the parallax problem and ensuing shadows. The shutter speed is 1/50 of a second and the aperture is determined by the film speed and watts/second output of the electronic flash. A small attachment on the ring adapter gives enough light to permit focusing through the camera before the flash is tripped.

DISCUSSION.

With the advent of modern histochemical techniques, especially for the study of ground substances and connective tissue

*Manufactured by A. Klenk Co., Maspeth, Long Island, N. Y.

formation, there are new methods available for the study of many tumors, including juvenile angiofibroma. The studies which have been presented in this thesis should be repeated and re-evaluated in all future cases, especially in the light of the newer staining techniques. Delarue, et al.,[68] and Weisskopf and Burn[33] have shown variations in staining and the quantity of metachromasia demonstrated by these histochemical techniques applied to the nose and nasopharynx. It becomes obvious that if these studies and investigations are to continue and be productive, pre- and post-treatment specimens should be obtained. Pre-treatment, preoperative biopsies usually produce significant hemorrhage, and post-therapy operative removal produces hemorrhages of major proportion. It is, therefore, felt that treatment can best be obtained at large clinics or university centers where adequate blood, selected anesthesia, and experience in handling these particular tumors are available. These resources, plus a laboratory that is capable of and interested in further study of this interesting tumor, make an ideal combination.

The diversity of the microscopic appearance of this tumor from a thin, myxomatous stroma to a dense, collagenous one, or from a young, budding capillary to a mature blood vessel, might well produce considerable speculation as to the significance of the appearance of a single high-powered field. It is, therefore, necessary to explore several sections of the tumor to select that area which appears representative. Since both androgens and estrogens induce involution and both produce a similar type of response in the microscopic appearance of the tumor, it would appear that the basic physiologic pathology is a dysfunction of the pituitary and that either sex hormone so administered tends to inhibit some aspects of the pituitary function. This, in turn, leads to the change in the ground substance and the involution of the tumor. It is felt that the angiofibroma is basically a desmoplastic or connective tissue response of the nasopharyngeal periosteum to a hamartomatous ectopic nidus of vascular tissue, probably of the inferior turbinate type. Its growth may start when the pituitary activity is first altered by the appearance or elaboration of the male sex hormone. Since male and female hormones exist in both sexes, it is probably the alteration of the

relationship or configuration between these hormones and the pituitary which permits this tumor to make its nearly exclusive nasopharyngeal appearance in the male.

It is recognized that several unproven propositions exist herein; however, the tumor itself is rare; it is not possible to produce it in an animal; and embryologic studies of the nasopharynx to show the origin of the tumor would be nigh futile, since it is not possible to know which of the thousands of the nasopharynges might contain the vascular tissue in question. Despite these unproven assumptions, the accumulation of clinical and experimental data on the diverse aspects of the problem appear to make the stated hypothesis a real possibility.

It is not expected that estrogen therapy would obviate the necessity for surgery, but it can be expected to decrease the amount of bleeding and cause some degree of involution. The use of female sex hormones to make a male more female carries with it some annoying physical and psychological reactions. There is occasional enlargement of the breast and in some young men a distinct loss of libido. These possibilities should be explained to the patient or the parents of a patient prior to instituting therapy. The patient in Case 3 was a young married man who reacted to the libido-robbing medication and said, "Doctor, your pills are real strong but my wife was stronger." About three months after therapy was discontinued on this patient, his wife conceived and later delivered a healthy child. A study of this case would seem to indicate that the sex life of the patient is only temporarily interrupted, and apparently no permanent damage is suffered by this modality of treatment. A larger series of the effect of female hormones on the male would be most enlightening.

Half of the cases reported here were located on the right; the other half on the left. There appeared to be no predilection for the left side as is suggested by Acuña.[52] This may be due to the difference in the number of cases reported.

Another interesting observation is the fact that three out of the four cases reported herein were distinct redheads of various degrees. Another patient recently seen in consulta-

tion by the author also had brown hair with a definite reddish cast to it. The significance of this observation is worthy of note but is indeterminate. Certainly these tumors occur in all ethnic and geographic groups, as attested by the voluminous world literature reporting their isolated cases; nonetheless, it would be interesting for other observers to note the skin and hair color in the appearance of future angiofibromas.

SUMMARY AND CONCLUSION.

Four cases of juvenile angiofibroma are presented. Two of the patients were treated with androgen and two with estrogen. Both hormones seem clinically to have an inhibiting effect to some extent on the tumor. The effect of estrogen appears to be considerable, with microscopic proof presented with pre- and post-treatment slides to show the maturing effect of the female sex hormone. It is hypothecated that since both hormones affect the maturity of this tumor, the mode of action is *via* the alteration of the pituitary activity. The terminus of action is in the ground substance and connective tissue of the tumor. It is proposed that this tumor is basically vascular and that the fibrous tissue component is a desmoplastic or connective tissue response to ectopic, sex-sensitive, vascular tissue like that found in the inferior turbinate.

The treatment of these tumors with estrogen is not a substitute for other modalities of therapy but a supplement in an attempt to decrease the vascular bed and help to mature the tumor.

Emphasis is placed on the necessity for future endocrine and histochemical studies of the ground substance to augment the basic understanding of this oncologic process.

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ADENO-TONSILLECTOMY AND DEAFNESS IN CHILDREN.*†

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The indications for adeno-tonsillectomy have remained the same over the years, only the interpretations and applications of these indications have varied, according to the individual physician. For that reason there has been an ebb and flow in the number of these operations performed, seasonally and otherwise.

Unfortunately, there have been times when logic has been swayed by fetishism in the minds of certain extremists. The most recent instance of this pseudo-hysteria is the persistance of the practice of not removing the tonsils and adenoid during certain months designated by the epidermiologists as the "polio season," regardless of the low numerical incidence of poliomyelitis cases at these times.

As a consequence, we have encountered innumerable patients with histories of repeated otitis media who are in grave danger of a permanent loss of hearing, because the operations would not be performed during the summer months, and could not be performed during the months of acute respiratory infections, at which times there is a much greater risk of serious complications than there is during the statistical "polio season."

Among the many indications for the removal of the tonsils and adenoid in children, difficulty in hearing has probably received the least attention by the general practitioner and the pediatrician, unless it is so very marked that it is too obvious to be overlooked.

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†From the Clinics of Firmin Desloge Hospital and the Cardinal Glennon Memorial Hospital, Department of Otolaryngology, St. Louis University School of Medicine, through funds derived from the Stuever Memorial Fund of the Department. The audiometric studies were performed by Mrs. Nancy Schlenk and Miss Josephine Murphy.

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Such remote consequences as inattention at home or in school, giving rise to situations of friction, social maladjustments, poor scholarship problems, or at times the more serious question of alleged personality changes of psychogenic origin in a child, are too frequently not recognized as possibly due to the inability of the child to hear adequately or to distinguish properly what is being said.

The physician's approach to such a child is often a negative one in the light of the absence of a voluntary history by the

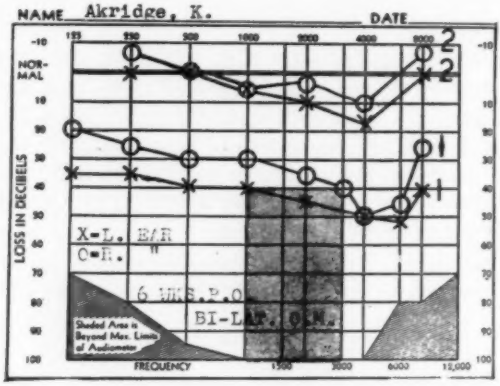

Fig. 1. Age 9; hearing poor 3 years; bilateral otitis media often. (1) Pre-operative; (2) six weeks post-operative audiograms. X = Left ear. O = Right ear.

patient, parent or teacher, of hearing difficulty. Positive questioning will more frequently elicit the desired information, although in certain instances this is not obtained until revealed by the pure-tone audiogram and confirmed by the discrimination tests, if feasible.

We realize the great value of the routine group audiometric tests being practiced in many of the public and parochial schools in recent years, in alerting teachers and parents to obvious hearing defects in school children; however, the circumstances under which these tests are conducted necessarily preclude the detection of less marked changes in hearing

which may be significant as trends toward progressive types of deafness. They may be ignored in the evaluation of the audiograms by individuals who are not conversant with such minor deviations from the normal. Such audiograms should be read and interpreted by otologists, if possible.

It is disheartening to the otologist to encounter child after child of 2 to 5 years of age with enormous tonsils, and with naso-pharynx filled with adenoid tissue which completely blocks both choanae, who is compelled to endure this physio-

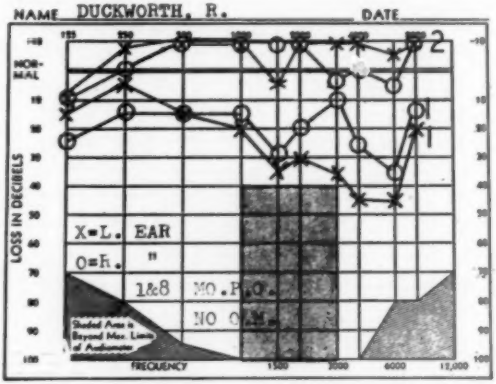

Fig. 2. Age 7; hearing poor 4 years; no otitis media. (1) Pre-operative and (2) one and eight months post-operative audiograms. X = Left ear. O = Right ear.

logical impasse for the sole reason that it must wait until it reaches the age of 5 or 6 years to have the tonsils and adenoid removed "because this lymphoid tissue *must* have some function."

That this lymphoid tissue has a function we must all acknowledge, and we do recognize the fact that some strides have been made in efforts to determine this function; however, the absence of this tissue does not preclude the continued similar function of lymph glands and other lymphoid tissue throughout the body.

Most investigators point up the fact that lymphoid tissue

is somehow involved in the formation of antibodies. Plasma cells, reticulo-endothelial cells and lymphocytes have been considered as stimulants or precursors of such antibodies. Schenck[1] aptly summarizes the plasma cell theory of antibody formation as follows: "The plasma cell appears to be the only cellular element in lymphoid tissue capable of synthesizing antibodies and Gammaglobulin. Lymphoid tissue is the site of antibody formation and the lymphoid tissue of Waldeyer's ring contains all of the cellular constituents essential for the

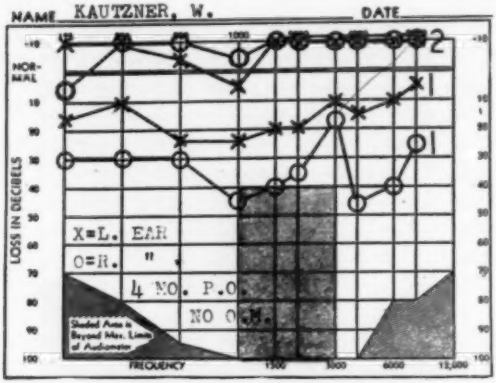

Fig. 3. Age 7; hearing poor one year, plus; no otitis media. (1) Pre-operative and (2) four months post-operative audiograms. X = Left ear. O = Right ear.

manufacture of humoral immune bodies. Lymph nodes and other lymphatic tissue appear to be the birthplace and graveyard of lymphocytes as well as the source of antibodies.

"The strategic position and structural modifications of the lymphoid tissues of Waldeyer's ring suggest that the prime function of this tissue is the formation of antibodies and other Gammaglobulins"; nevertheless, however much we respect and wish to preserve this function, when the tonsils and adenoid tissue become so greatly hypertrophied from repeated infections, allergic states or dietary maladjustments, that they assume the proportions of tumors with a verisimilitude of local malignancy, we would not be justified in deferring their

removal any more than we would any other tumor of similar local malignancy, regardless of the age of the patient.

This state of local malignancy comprises the more or less complete obstruction of the nasal airway, thus causing the mechanical interference with the post-nasal drainage from the nasal sinuses, and with proper aeration of the eustachian tubes and middle ears; also, the harboring of infectious bacteria in the crypts of the adenoid and tonsil predisposes to extension of infection into the middle ears and paranasal sinuses.

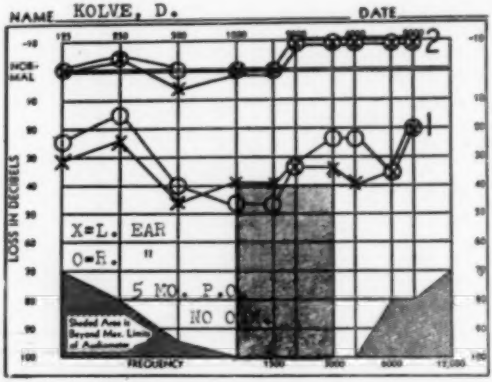

Fig. 4. Age: 6 years; hearing poor 1 to 2 years. (1) Pre-operative audiogram, and (2) five months post-operative audiogram. X = Left ear. O = Right ear.

This extension of infection into the middle ear may take place not only through the lumen of the short, straight and well open eustachian tube, but also through the subepithelial tissue of the mucosa of the tube and middle ear, causing the congestion and closure of the tube which isolates the infecitous material in the middle ear.

In discussing the removal of lymphoid tissue from the nasopharynx for the relief of deafness, one must necessarily consider irradiation of the nasopharynx with radium as a purposeful adjunct.

This method, using 50 mgm. of radium, shielded with 0.3 mm. of monel metal, on an applicator for transnasal introduction into the nasopharynx, originated with Crowe at Johns Hopkins Hospital in 1924.[2]

In 1948 Crowe[3] reported favorably on this method in a paper read before the American Otological Society. Following this and other more detailed reports, the nasopharyngeal radium applicator was used quite generally.

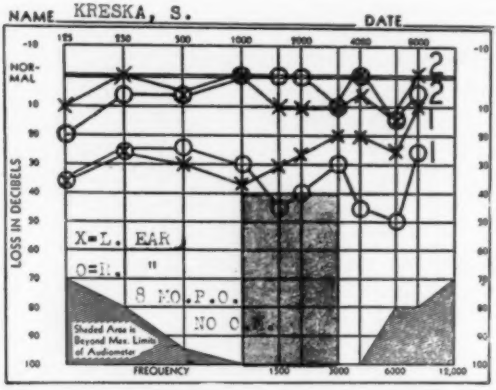

Fig. 5. Age: 6 years; hearing poor for 3 years. (1) Pre-operative audiogram, and (2) eight months post-operative audiogram. X = Left ear. O = Right ear.

In 1954, Bordley and Hardy[4] of Johns Hopkins reported at the meeting of the American Otological Society, a greater improvement in hearing in unoperated cases with irradiation, than in the non-irradiated cases; however, their optimism was not shared by the discussors.

Among the objections raised were: *1.* Too large a dosage of radium for the safe toleration by the nasopharyngeal mucosa, and *2.* the possible carcinogenic effect of this exposure to radium. These comments I shall leave open to discussors in search of a possible explanation for the apparent lack of usage of this expedient in recent years.

In 1956 Adams,[5] of Birmingham, England, reported up to 75 per cent improvements in hearing following the use of radium in non-benefited operated cases.

In comparing the relatively prompt results obtained by thorough surgical removal of tonsils and adenoid, with the protracted questionable results claimed, in the quasi eradication of the adenoid and exuberant lymphoid tissue in the nasopharynx, using irradiation, the latter procedure seems to be an unjustifiable compromise when the importance of restoring hearing as soon as possible is the ideal objective.

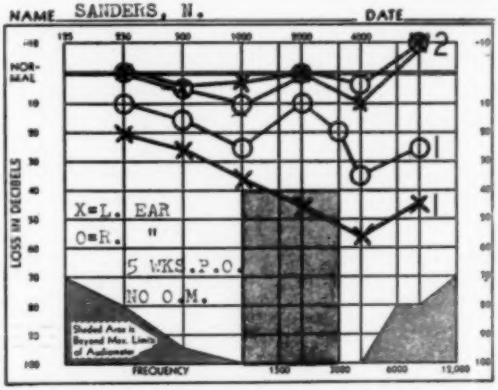

Fig. 6. Age: 9 years; hearing poor 2 years, plus. (1) Pre-operative, and (2) five weeks post-operative audiograms. X = Left ear; O = Right ear.

This presentation is intended to stress the importance and the significance of the removal of hypertrophied tonsils and adenoid in patients with or without a complicating otitis media, who may have hearing defects as a result of infections of such tonsils and adenoid.

The 86 children, between the ages of 6 and 13 years included in this study, were recommended for adeno-tonsillectomy for local and constitutional symptoms as well as for hearing defects. Pre-operative audiometric and tuningfork studies were done within a few days of the operation and

repeated in four to several weeks postoperatively, according to the degree of cooperation by the parents. Discrimination audiograms were not done routinely, on account of the ages of the patients.

The history of poor hearing of varying degrees and lengths of time, as given by the mother or patient, occurred in 21 of the 86 patients (24.4 per cent). When this figure was allocated it was found to apply almost solely to the group of 41 patients (47.7 per cent), whose audiograms revealed hearing losses in one or both ears, an incidence of 51.2 per cent, in contrast to the remaining 45 patients (52.3 per cent) whose audiograms were normal, both pre- and post-operatively.

In this group of 41 patients the hearing improved to normal in 26 (63.4 per cent) within four weeks to eight months, as evidenced by several audiograms and by the absence of a subsequent history of diminished hearing.

In the group of 15 patients (36.6 per cent) whose hearing had not improved appreciably, there were four who had suffered a nerve or a mixed deafness. The remaining 11 were cases of conductive deafness; therefore, in the 37 cases of conductive deafness, there was improvement in 26 (70.3 per cent), and little or no improvement in 11 (29.7 per cent).

The incidence of one or several attacks of otitis media must always be considered as a possible deterrent to improvement in hearing, even though the adenoid and tonsils have been thoroughly removed. The history of otitis media seemed to have a more significant bearing on the lack of hearing improvement in the 15 cases. In this group, it occurred in 66.6 per cent, while in the 26 (70.3 per cent) definitely improved cases it occurred in only eight or 30.8 per cent.

When we consider the definite improvement in hearing which followed the adeno-tonsillectomies in a relatively short time we ask ourselves, should we not strive to help these children regain their hearing at an earlier age?

The average age of these children was 7.8 years at the time

of their operations, and the average length of time that they were known to have had poor hearing was 2.4 years, during which time they had suffered many attacks of otitis media, and had probably experienced innumerable difficulties in adjusting at school and at home from their inability to keep in adequate contact with their environment during these most important formative years.

SUMMARY.

In a review of the incidence of poor hearing in 86 children who were undergoing adeno-tonsillectomy for reasons of health, we found that 45 (52.3 per cent) had normal hearing, audiometrically and clinically, and 41 (47.7 per cent) had poorer hearing. Among this 47.7 per cent, hearing was restored to normal in 63.4 per cent, and not improved in 36.6 per cent. The important factor in the non-improvement cases was probably attacks of otitis media, which occurred in 66.6 per cent over a period of several years.

The average age of patients at the time of operation was 7.8 years. The average length of time of the history of poorer hearing, with or without otitis media, was 2.4 years.

Total—86.		Otitis Media	
	No. of Cases		No. of Cases	
Audiogram, normal	45 — 52.3 per cent		4 — 0.9 per cent
Audiogram, not normal	41 — 47.7 per cent		18 — 43.9 per cent
Complaint poor hearing	21 — 51.2 per cent		10 — 47.6 per cent
Hearing improved	26 — 63.4 per cent		8 — 30.8 per cent
Not improved	15 — 36.6 per cent		10 — 66.6 per cent

CONCLUSIONS.

Judging by the definite improvement in hearing which followed adenoidectomy or adeno-tonsillectomy in children with poor hearing, with or without the complication of otitis media, we feel that it is advisable to perform this operation as soon as it is justified by the clinical conditions, regardless of the age of the patient. Procrastination may lead to irreparable damage to hearing.

It should be our responsibility as otolaryngologists to impress forcefully upon the general practitioner, the pediatrician, the parents, and the social service worker, the significance of the earliest complaint by a child, or the earliest impression of the parent of difficulty in hearing.

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SIXTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST.

The Sixth International Congress on Diseases of the Chest will be held at the University of Vienna from August 29 to September 1, 1960.

ENDOCRINE ASPECTS OF MENIERE'S DISEASE.*

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Ménière's disease, or endolymphatic hydrops as we prefer to call it in view of its known pathology, is one of the most difficult therapeutic problems in otology. Because of the fluctuations in hearing so characteristic of this condition the symptoms, at least in the earlier stages are reversible, and we cannot accept a nihilistic therapeutic attitude, nor can we advise destructive labyrinthine surgery except as a last resort; on the other hand, the medical treatment of this condition has been disappointing in many cases.

The problem of hydrops is added to by the apparent increase in frequency of this type of hearing impairment. Of the new patients seen in our office because of impaired hearing during the year 1958, 12 per cent were diagnosed as being the result of endolymphatic hydrops. In addition to these new cases, we see a good many cases of hydrops following fenestration and stapes mobilization surgery. In a study made in 1950,[1] 10 per cent of the fenestration patients followed in our office practice had developed definite symptoms of hydrops, beginning usually many months or years after a successful fenestration operation, with one or more of the four cardinal symptoms of hydrops; namely, an abrupt drop in hearing with fullness, roaring tinnitus and dizziness. The fact that the hearing returned to its previous level and the other symptoms were relieved after administration of dilute histamine, was taken as evidence that the drop in hearing was due to hydrops and not to closure of the fenestra or nerve degeneration.

I might mention that our routine medical management of hydrops[2] consists of specific therapy of any coincidental

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allergic symptoms; a low salt diet, sometimes combined with the administration of ammonium chloride or potassium chloride; omission of smoking; and the administration of very dilute histamine according to the method of Hansel.[3] Histamine has been the most successful of these therapeutic agents, particularly in early cases where the hearing level was fluctuating markedly, and in the postoperative fenestration and stapes mobilization cases.[1]

I also call your attention to an interesting observation in cases of stapes mobilization that are revised. In a fair number of these there is an outpouring of perilymph, the moment the footplate is cracked, that far exceeds the amount of perilymph observed at the first operation. This suggests that the hydrops that occurs postoperatively may involve an increase in the amount of perilymph as well as in the amount of endolymph. The term labyrinthine hydrops may indeed be more appropriate than endolymphatic hydrops.

We became interested in the endocrine aspects of Ménière's disease through our interest in allergic problems and our more recent interest in the enzymatic concept of allergy. In the provocative little book by Z. Z. Godlowski entitled "Enzymatic Concept of Anaphylaxis and Allergy," published in 1953,[4] the rapid advances made in recent years in cellular physiology and protein metabolism are brought together in a new concept of the allergic state. This new concept explains many of the apparent contradictions and paradoxes of clinical allergy that were never explained by the antigen-antibody mechanism. Boiled down to the fewest possible words, the enzymatic concept of allergy is as follows:

The normal living cell is not at all the inert blob of cytoplasm that we are accustomed to seeing in the fixed stained microscopic slide. Rather, the living cell is in a state of constant and tremendous metabolic activity, vividly seen in phase-contrast cinematography of living cells in tissue culture. Around the nucleus we can see the mitochondria squirming and dancing, with hectic motion of granules and inclusions that appear and disappear. The cell membrane is in constant amoeboid undulatory movements, reaching out and drawing into itself nutrients from the surrounding fluid medium. We

know that within the cytoplasm complex protein molecules are in a continuous process of being built up and torn down by means of enzymes operating through the mitochondria. These enzymes which control protein catabolism and anabolism are produced by the cell itself. When a new foreign protein is carried to the cell by the blood stream, there is produced within the cell a new specific enzyme to proteolyze this particular protein molecule and break it down into non-toxic amino acids. These amino acids are then utilized as food to build new protein. The newly formed enzyme is called *adapted or induced enzyme*, and once produced it remains in the cell ready to catabolize any new molecules of that particular foreign protein that may come along. This, then, is the *normal* response of healthy living cells to the minute quantities of foreign protein that continually reach the cell via the blood stream.

In the allergic individual a different course of events occurs. Due to an inherited or acquired deficiency in enzyme production, or due to the presence of an enzyme inhibitor, the induced enzyme that arises when a foreign protein enters the cell is one that fails to produce all-or-none proteolysis to harmless non-toxic amino acids. Instead, this abnormal enzyme produces *partial proteolysis* with the production of highly toxic compounds, including *histamine*, heparin, proteoses, serotoxin, acetylcholine, leukotaxine, pyrexin, necrosin, leukogenic factor, bradykinin, serotinin, and still other as yet unidentified compounds. These toxic materials liberated within the cell each time more of this particular foreign protein enters the cell, produce the pathologic and clinical manifestations of the allergic reaction, with smooth muscle spasm, capillary dilatation and increased permeability, and edema.

Thus we see that the *etiology* of the allergic state is the production of an abnormal type of enzyme. This may be due to an inherited defect of enzyme production, or to enzyme inhibitors such as infections, antibiotics, coal-tar products (salicylates, etc.), or endocrine deficiency. It is known that the action of thyroid hormone in particular, is closely related to the cytoplasmic mitochondria. When there is a deficiency within the cell of thyroid hormone the formation of proteins

suffers, and since enzymes are proteins, the formation of the normal type of all-or-none proteolytic enzyme is deficient.

The relationship between endolymphatic hydrops and allergy has been noted by many authors, and is well documented in the very fine monograph by Henry L. Williams[5] on Ménière's disease. It is interesting that in our office force of 17 individuals, no less than six of us have had one or more typical episodes of endolymphatic hydrops. All six of us are allergic to certain foods or inhalants, although our labyrinthine symptoms have not been associated with an allergic upset in most instances.

In 53 cases of endolymphatic hydrops that failed to respond to the usual medical regime, including dilute histamine, the patient was referred for endocrine evaluation by the author of the Enzymatic Concept of Allergy.[4] Of the 53 patients referred, 27 failed to return for adequate follow-up, while 36 followed the recommended therapy and returned for evaluation of the results. Of these, 26 failed to show greater improvements in hearing or other symptoms than these same patients had experienced in spontaneous remissions and fluctuations, while in ten, or 28 per cent, the results of endocrine therapy were positive with definite improvement or complete relief in one or more of the cardinal symptoms. Several of these cases were very dramatic, indeed, with results sufficiently definite to satisfy the most skeptical critic.

In the great majority of cases the endocrine dysfunction was the hypometabolic syndrome of deficient utilization of thyroid hormone at the cellular level. These patients have a normal protein-bound iodine level indicating normal production of thyroxin, but they have deficient utilization of thyroid hormone by tissue cells apparently due to inability of the cells to break down thyroxin to tri-iodo-thyronine. The deficiency is evident in a lowered sedated basal metabolic rate, and in symptoms of hypothyroidism such as dry skin, thin hair, inability to lose weight, edema, constipation and fatigue. The symptoms are not improved to administration of thyroxin or desiccated thyroid, but they are relieved by tri-iodothyronine.

Representative cases are the following:

Miss M.J.C., age six, complained of complete deafness in the left ear for one year, fluctuating hearing in the right ear for three months. Weekly injections of histamine 1-100,000,000 with drops of 1-10,000,000 dilution under the tongue twice daily, resulted in a remission in the fluctuating deafness in the good ear, but each time the histamine was omitted the fluctuations recurred. A thyroid deficiency was suspected and confirmed by an endocrinologist. On desiccated thyroid the symptoms were relieved for eight years. She then returned because of a recurrence of the fluctuating deafness, despite large doses of thyroid extract. Endocrine evaluation revealed the hypometabolic syndrome. On tri-iodo-thyronine 100 mcgm twice daily, there was a complete remission in auditory symptoms as well as in the hypometabolic symptoms.

Mr. G.B., age 58, complained of progressive hearing loss in both ears for 12 years, with occasional attacks of vertigo. On the usual medical therapy including dilute histamine there was no improvement. Endocrine evaluation: hypometabolic syndrome, despite having taken desiccated thyroid for years. Therapy: tri-iodo-thyronine 5 mcgm t.i.d. resulted in a gradual improvement in hearing and a marked improvement in the ability to understand speech. Due to business pressure he resumed smoking, and had a typical attack of vertigo, but hearing remained improved.

Dr. L.A., was first seen at the age of 58 with complete deafness in the left ear for 25 years, and fluctuating hearing in the right ear for several years, gradually increasing in severity. Medical therapy, including dilute histamine of doubtful benefit. Endocrine evaluation: hypometabolic syndrome. Patient given bicillin for a chronic nasopharyngitis and tri-iodo-thyronine, increasing to 25 mcgm t.i.d. Within three days the hearing in the right ear returned to normal, with cessation of roaring, dizziness and hearing fluctuation. After 18 months of complete absence of relapse he omitted tri-iodo-thyronine and after two weeks developed vertigo, tinnitus and a marked drop in hearing. Sedated B.M.R. now –20 in two tests, whereas while on the tri-iodo-thyronine it had been normal. Resumed the medication 36 mcgm daily, and within five days the hearing returned to normal and stabilized with disappearance of tinnitus and vertigo.

CONCLUSIONS.

The enzymatic concept of allergy and related disorders offers a rational explanation for the etiology of endolymphatic hydrops, the increased production of endolymph being the result of abnormal enzymes in the epithelial cells of the stria vascularis. Toxic products of incomplete proteolysis due to these abnormal enzymes cause capillary dilatation and permeability in the stria vascularis. Dilute histamine injections probably serve to stimulate the production of the enzyme histaminase.

In 28 per cent of a small series of cases of hydrops that failed to respond to dilute histamine, correction of a deficiency

of thyroid metabolism resulted in a greater improvement in symptoms than would probably have occurred in the normal fluctuations in these cases. The usual deficiency was the condition known as the hypometabolic syndrome with normal P.B.I. but lowered basal metabolic rate when this was taken after sedation. In this condition desiccated thyroid is not effective, whereas tri-iodo-thyronine can relieve the hypometabolic symptoms.

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TWO-FREQUENCY AUDITORY SCREENING: A CLINICAL EVALUATION.*

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In 1957, House and Glorig[1] reported studies which showed that in 98.5 per cent of individuals, hearing loss of 4000 cycles per second was equal to or greater than that for lower frequencies. As a result of this study they proposed a system of auditory screening that used the single frequency of 4000 cps. Simple, self-contained battery-operated instruments were developed for this purpose. These are available in single-frequency models that produce a tone of 4000 cps and in two-frequency models that provide tones of 4000 cps and 2000 cps. Both instruments provide two intensity levels: 35 db and 15 db.

The purpose of single or two-frequency auditory screening is to provide a rapid method of determining those persons whose hearing is defective and who should have more extensive study. The advantage of such a method is obvious when one contemplates testing large groups of individuals as in schools or industry. Screening audiometry is also proposed for use by physicians other than otologists to discover those persons who have hearing problems and who should be referred to the otologist for further study.

Our practice is one of general otorhinolaryngology. The volume of work is such that pure-tone threshold audiometry for every patient is impractical. Audiometric examination is done on those patients whose symptoms are related to the ear or hearing, and in certain groups being examined for in-

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dustry. It is not done on patients whose symptoms involve only the nose or throat.

Auditory screening of patients who would not normally have audiometric examination offers the advantage of detection of otherwise unrecognized hearing losses, and also provides a minimal record of hearing for future reference in the event the patient subsequently loses hearing. Both are real advantages, which led to our decision to screen the hearing of each patient coming to our department.

We selected a two-frequency, two-intensity screener with a single earphone. This instrument provides tests at 4000 and 2000 cps at intensities of 35 and 15 db. We consider screening at two frequencies more useful for our purpose than screening at a single frequency. Four thousand cps has the advantage of demonstrating a high percentage of all hearing losses and of relative immunity to masking from the ambient noise of the average office. This frequency alone is unduly selective when persons in the presbycusis age are tested. Many persons have losses at 4000 cps whose hearing for speech is not significantly affected. The addition of a screening test at 2000 cps gives information that aids in determining which patients have trouble hearing conversation. The single-earphone instrument was selected for its simplicity and rapidity of operation. The patient holds the earphone to his ear while the attendant operates the instrument.

In our practice the screener is operated by the attendant who shows the patient to the examining room. The test is done in the examining room with the door closed. The rooms have no sound conditioning, although the sound of feet is minimized by cork flooring. The most prominent sound within the room is that of air flowing through the ventilating ducts. Outside the room are sounds arising from conversation of patients in the corridor and intermittently from instruments being cleaned and placed in the sterilizer. Outside windows are sealed. The level of ambient noise in the room measured with the General Radio Sound Level Meter set at the "A" position approximates 42 db but peaks to 60 db at times. Each ear is tested, first at 4000 cps, then at 2000 cps. The tone is

presented first at 35 db, then at 15 db. The patient is instructed to report each time the tone is heard.

The personnel who operate the auditory screeners have not had previous experience in testing of hearing. They are carefully instructed in the operation of the instrument. This is a very simple procedure which consists of turning the frequency selector to one of two positions for 4000 or 2000 cps. The tone is presented by pressing one button for 35 db, another for 15 db. An undesirable click is produced if the on-off button is depressed quickly, but can be avoided if the button is depressed slowly. Possibility of error in operation is reduced to a minimum by the simplicity of the instrument.

Audiograms were carried out by a qualified audiologist (L.D.H.) and a technician who had had 15 years' experience in audiometry. The tests were done on Maico E-2 audiometers that had been calibrated at the factory within the past year, and that had been further checked at threshold by comparison with a newly calibrated instrument, a group of normal-hearing individuals being used as test subjects. All audiometry was done in sound-treated rooms in which the ambient noise level as determined by the General Radio Sound Level Meter was 32 db in one room and 38 db in the other, with the sound level meter set at the "A" response position.

The records of 758 patients were available for review. This was a selected group in which the majority complained of a hearing problem. In order to evaluate the results of screening on normals, 90 additional patients who were unaware of a hearing problem were tested. The auditory screen revealed no loss in 53 of these patients, while in 37 the 4000 cps tone was not heard at 15 db.

The pure-tone threshold data were analyzed to determine the number of instances in which the pure-tone air-conduction threshold at 4000 cps was as great as, or greater than, the threshold at 500, 1000 and 2000 cps. The threshold at one or all frequencies from 500 to 2000 cps was higher than the threshold at 4000 cps in 171 (20.2 per cent) of 848 audiograms studied. The maximum by which the threshold for lower frequencies exceeded the threshold at 4000 cps was 5 db in

TABLE I.

Audiograms in Which the Threshold at 500, 1000 or 2000 cps Exceeded the Threshold at 4000 cps Among 848 Audiograms.

	Number	Per cent
Total	171	20.2
Exceeded by:		
5 db	69	8.2
10 db	40	4.7
15 db	26	3.1
20 db or more	36	4.2
Significant errors (10 db or more)	102	12.0

TABLE II.

Instances in Which Screen Showed Normal Hearing (93 Patients).

Screen and Audiometer	Number
Agreed	89
Disagreed	4
By: + 5 db	3
+15 db	1

TABLE III.

Screen Showed Loss of 15 db at 4000 cps (67 Patients).

Screen and Audiometer	Number
Agreed	24
Disagreed	43
Screen not heard at level heard on audiometer	10
By: − 5 db*	13
−10 db	11
−15 db	5
+ 5 db	1
+15 db	3

*− = screen showed poorer hearing than audiometer; + = screen showed better hearing than audiometer.

69 instances, 10 db in 40, 15 db in 26, and 20 db or more in 36. Differences of 5 db can be considered within the limit of error in audiometry. Differences greater than 5 db are considered significant. Differences of 10 db or more were observed in 102, or 12 per cent, of the audiograms studied (see Table I).

The auditory screen showed no loss in 93 of the 848 patients. The audiogram agreed with this finding in 89 (see Table II). The screen showed loss of 15 db for the tone of 4000 cps in 67 patients. The audiometric threshold confirmed the screen in 24 instances (see Table III).

The findings of the auditory screening were confirmed by the pure-tone threshold audiogram in 473, or 55.8 per cent, of the 848 patients. Errors occurred in 375 instances. The screen indicated better hearing than the audiometric threshold in 115 instances, less hearing in 243 instances. Multiple errors of similar class (better or worse) appeared on 95 cards. Crossed errors (screen both better and worse) appeared on 17 cards. Where multiple errors occurred the card was classified according to the error of greatest magnitude.

TABLE IV.

Instances in Which Screen Showed More Hearing Than Audiometer.

	Number	
By: + 5 db	48	
+10 db	23	
+15 db or more	44	
Significant errors (10 db or more)	67	(7.9%)

TABLE V.

Instances in Which Screen Showed Less Hearing Than Audiometer.

	Number	
Screen not heard at level heard on audiometer	80	
By: – 5 db	70	
–10 db	60	
–15 db or more	33	
Significant errors (10 db. or more)	93	(11.0%)

Variations of plus or minus 5 db are generally considered to be within normal limits of error in audiometry. Errors of 10 db or more occurred in 160 instances (18.9 per cent). In 67 patients (7.9 per cent) the screen showed more hearing than the audiogram (see Table IV). The magnitude of the error ranged to 85 db. In this instance, a patient whose audiogram showed no hearing in one ear was reported as hearing 15 db on the screen test. In 93 patients (11.0 per cent) the screen showed less hearing than the audiogram (see Table V). The maximum error in this direction was 20 db.

COMMENT.

Study of this series of audiograms indicates that a single-

frequency screen at 4000 cps is not a valid index of maximal loss. The difference between our results and those reported by House and Glorig is explained in part by the relatively high proportion of patients with conductive lesions and end-organ lesions among those tested.

Comparison of the results of auditory screening and pure-tone threshold audiometry done under the conditions described reveals a high proportion of error. Repeated comparison of the screeners and the audiometers by loudness-balance tests using normal ears failed to reveal significant differences in the calibration of the instruments. This, plus the fact that the screening test showed both more and less hearing than the threshold tests, suggests that the discrepancies resulted from errors of technique and of recording. The threshold tests were done by experienced personnel using well-standardized techniques. The screening tests were done by inexperienced personnel who had been instructed in use of the instrument but who lacked the experience necessary to question the results of their own tests. We assume that the errors are principally in the results of the screening tests.

Possible sources of error in which the screen shows more hearing than the threshold test are a click present when the on-off button of the screener is depressed and response of the patient to the examiner's voice when asked "Do you hear now?". The first error can be reduced by care in depressing the button and by occluding the ear not being tested. The second can be avoided by better instruction of the operator in the technique of hearing tests. Possible sources of error in which the screen shows less hearing than the threshold test are masking by ambient noise, which should have little effect at 4000 cps, improper positioning of the earphone by the patient, and poor instruction of the patient in the nature of the test.

Use of a screener equipped with binaural earphones would reduce errors due to ambient noise or clicks in the instrument. Adjustment of the head set would require more time, and the addition of another switch to the screener would add to the chance of designating the wrong ear when the results are recorded.

Our experience indicates that auditory screening is not a procedure that can be accurately performed by inexperienced personnel after minimal instruction. The instructions given to members of our office staff in the use of the screener were deemed adequate. In addition, as errors were noted they were often called to the attention of the attendant operating the screener. Many times, obvious errors were rechecked by the consultant in the presence of the attendant and different results noted. Despite these precautions, differences of 10 db or more between results of the screen and threshold audiometry were noted in 18.9 per cent of the records studied. This study suggests that the operator of an auditory screener must have both adequate instruction and experience if the results of the test are to be reliable. On the basis of our experience there is doubt as to the value of this procedure in situations in which the operators of the screening instruments fail to receive abundant experience as well as some objective evaluation of the results obtained.

SUMMARY AND CONCLUSIONS.

The results of two-frequency, two-intensity auditory screening were compared with the pure-tone, air-conduction threshold audiograms in 848 patients. Significant discrepancies appeared in 18.9 per cent of the records. It is believed that the majority of errors resulted from poor technique in the operation of the auditory screeners and in the recording of results.

ADDENDUM.

Continued comparison of the results of auditory screening with the results of pure-tone threshold audiometry has shown moderate improvement in the correlation between the two tests. Four hundred and sixty records were reviewed. Errors of 10 db or more were noted in 49 (10.7 per cent). The highest incidence of error occurs in tests done by assistants who are temporarily assigned to the department.

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PAPILLARY CYSTADENOMA LYMPHOMATOSUM OF THE PAROTID GLAND.*

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INTRODUCTION.

Non-tender swellings in the parotid region are usually caused by neoplasms. About 60 per cent of these are benign mixed tumors; another 30 per cent are malignancies arising in mixed tumors or as primary growths. The third common tumor is the papillary cystadenoma lymphomatosum. It was once considered rare; however, it accounts for about five per cent of all parotid tumors[14] and over 367 cases have been reported in the literature.[7] Examples of this tumor can be found in the files of most surgical clinics.

The tumor is composed of epithelial and lymphoid tissue. This feature is common to another lesion of the salivary gland from which it must be clearly distinguished; namely, Mikulicz's disease (the benign lymphoepithelial lesion). It is common practice to discuss these lesions together under the single designation, adenolymphoma; however, they are two distinct entities, both clinically and pathologically. This report is primarily concerned with the papillary cystadenoma lymphomatosum and will discuss Mikulicz's disease later in the differential diagnosis.

Hildebrand,[17] in 1895, was the first to describe the lesion. In a study of lateral cervical cysts and fistulas, he included a description of a lesion composed of both lymphoid and epithelial elements. He considered this a variation of a branchiogenic cyst, and suggested that it probably was derived from heterotopic entoderm.

In 1910, Albrecht and Arzt[1] established it as a definite

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pathological entity and separated it from branchiogenic cysts. They suggested the tumor arose from heterotopic salivary gland tissue found in lymph nodes of the parotid region.

In 1929, Warthin[32] made the first report in American literature; he described two cases in over 700 parotid tumors. He thought the tumor resembled the Eustachian tube in architecture and postulated its origin in a displaced anlage of the Eustachian tube. He proposed that the tumor be called papillary cystadenoma lymphomatosum; however, his name became associated with the lesion, and in this country it is commonly known as Warthin's tumor.

TABLE I.

Various Terms for Cystadenoma Lymphomatosum.*

1. Congenital epithelial cysts.
2. Branchial cyst of the parotid.
3. Cystadenoma of the parotid.
4. Papillary cystadenoma in lymph node.
5. Papillary intralymphonodular cystadenoma.
6. Branchiogenic adenoma of neck.
7. Branchiogenic papillary cystadenolymphoma.
8. Branchioma.
9. Epitheliolymphoid tumor of parotid.
10. Lymphoglandular cystoma.
11. Papillary cystadenoma with lymphoid supporting tissue.
12. Cystic papillary adenoma.
13. Papillary cystadenolymphoma.
14. Kyste Amygdaloide.
15. Tumeur amygdaloide.
16. Polykstiques: cystadenolymphoma parotids.
17. Adenoma branchiogenes cylindrocellulare cystium.
18. Papillary cystadenoma lymphomatosum.
19. Papillary cystadenoma.
20. Onkocytoma.
21. Orbital inclusion cyst.
22. Adenolymphoma.
23. Adenocysticum lymphomatosum.
24. Warthin's tumor.

*Chaudry, A. P., and Gorlin, R. J.: Papillary Cystadenoma Lymphomatosum (Adenolymphoma). "Amer. Jour. Surg.," 95:923, 1958.

Since that time a multiplicity of terms have been used to describe the lesion (see Table I). Each name reflects the author's opinion of the histogenesis of the tumor or tends to stress one or the other of its elements. This has made the subject appear complex and has led to some difficulties in classification of parotid tumors.

Grossly, the tumor is round or oval. Its surface has a slightly lobulated appearance produced by the cysts which may appear translucent through the thin, fibrous capsule. It is usually located in the lower part of the superficial portion

of the gland; it may be extracapsular or lie in the substance of the gland. In the deep portion of the gland, it displaces the normal tissue. It may be unicentric or multicentric. Its cut surface reveals a pink-grey tissue with cystic spaces filled with brown or straw-colored, gelatinous fluid.

Microscopically, the tumor has an easily recognized appearance given to it by the two types of tissue which compose it. An epithelial layer lines the cystic spaces and projects into

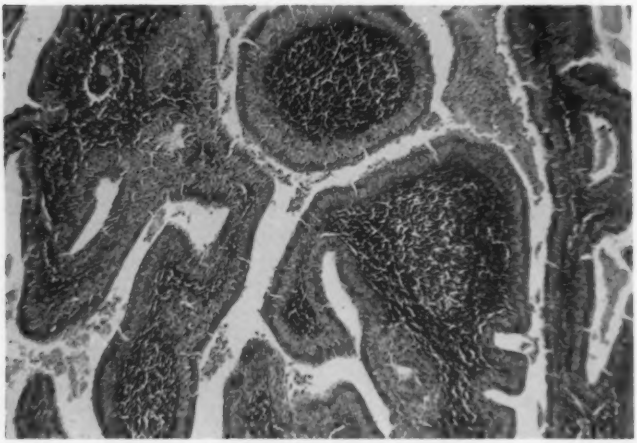

Fig. 1. Papillary cystadenoma lymphomatosum showing typical arrangement of papillae.

the lumen as multiple branching papillas. Cells of the epithelial layer are arranged in two rows. The inner cells are tall, columnar with oxyphilic cytoplasm. Their nuclei are arranged in an orderly fashion at the luminal end of the cells. They are not ciliated as Warthin thought. The outer or basal cells are polygonal and rest on a distinct basement membrane which separates them from the lymphoid stroma. The cystic spaces may be filled with branching papillas, or contain a granular material produced by the secreting epithelium and by debris of extruded mature cells.

Lymphoid tissue forms the supporting stroma of the tumor

and extends into the core of the papillae. Germinal centers are prominent. In some cases the essential architecture of the lymph node is preserved and the capsule, lymph sinuses and cortex can be identified.[2,31]

HISTOGENESIS.

The presence of both epithelial and lymphoid elements in the tumor, plus its occurrence limited to the parotid region,

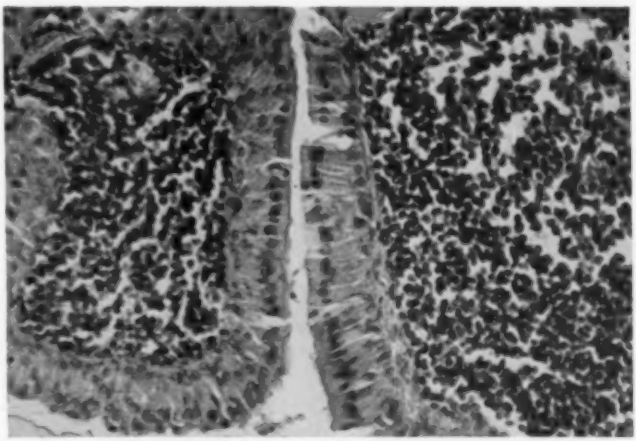

Fig. 2. Papillary cystadenoma lymphomatosum showing epithelial layer and lymphoid stroma.

has stimulated much speculation about its origin. The tumor has been thought to arise from: *1.* displaced pharyngeal entoderm;[17,32] *2.* Eustachian tube anlage;[32] *3.* branchiogenic cysts or fistulas;[17,29] *4.* aberrant salivary gland tissue in lymph nodes;[1] *5.* ectopic tonsillar tissue;[5,19] *6.* the orbital inclusion body of Chievitz;[20] and *7.* onkocytes found in salivary glands of adults.[15,18]

The branchiogenic theory of origin is not supported by any similarity between the epithelium of the tumor and that of branchiogenic cysts or fistulas. Branchiogenic cysts and fistulas are lined by stratified squamous epithelium or by

pseudostratified ciliated columnar epithelium, alone or in combination. Thompson and Bryant[31] could find no similarities in staining qualities or in nuclear arrangements between the branchiogenic epithelium and that of Warthin's tumor.

Warthin believed the tumor represented a developmental disturbance of the Eustachian tube anlage which later became neoplastic. His opinion was based on the misconception that the epithelium of the tumor was ciliated like that of the

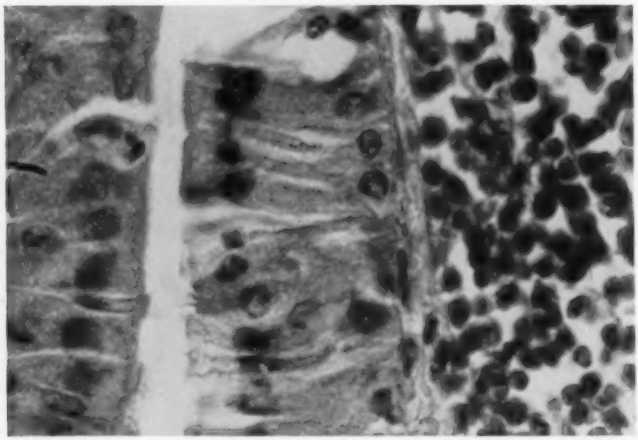

Fig. 3. Papillary cystadenoma lymphomatosum showing columnar cells, basal cells, and basement membrane.

Eustachian tube. It is agreed by most investigators that the cilia which Warthin described were artifacts.

The onkocytic theory of origin was proposed by Hamperl.[15] The onkocytes are cells which characteristically appear in salivary glands after the age of 30. They have an oxyphilic finely granular cytoplasm and nuclei rich in chromatin. The tumor was thought to have its origin in these cells. The theory does not explain the tumors which arise before the appearance of onkocytes in the young age group; furthermore, onkocytes have been found in other locations, but Warthin's tumors occur only in the parotid region.

The heterotopic salivary gland theory was proposed by Albrecht and Arzt[1] and has gained the widest acceptance. There are many facts which tend to support it: *1.* during embryonic development, the parotid gland, unlike the submaxillary, does not have a difinite capsule separating it from other tissues in the area; hence, some glandular tissue may become separated from the developing gland or become enmeshed in the lymphoid tissue developing in the same area; *2.* salivary gland tissue has been found frequently in the lymph nodes of

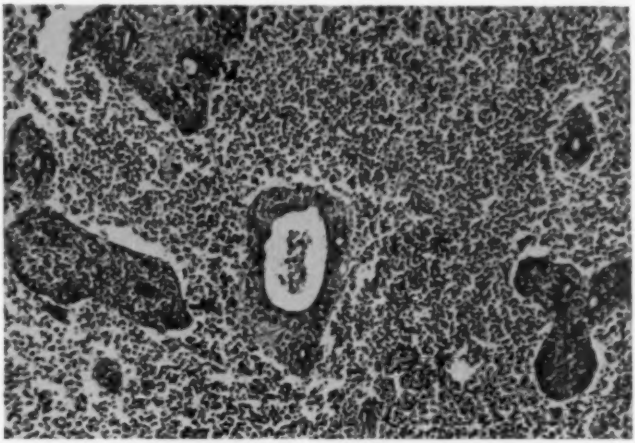

Fig. 4. Benign lymphoepithelial lesion (Mikulicz's Disease), showing epimyoepithelial islands, and lymphoid stroma.

the parotid region, both in fetuses and in adults;[13,31] *3.* tumor is found only in the parotid and periparotid region;[22] *4.* the lymphoid stroma of the tumor is not an infiltrate, but retains the normal characteristics of a lymph node; this indicates that the tumor arises within the lymph node;[3] and *5.* the cells of the papillary layer are similar to cells found lining the ducts of normal parotids.[31]

These observations support the theory of Albrecht and Arzt that the tumor represents a true neoplasm developing from

the ductal epithelium of aberrant salivary gland tissue trapped in lymph nodes of the parotid region.

CLINICAL COURSE.

The tumor usually presents as a non-tender swelling located in front of the lobe of the ear or just behind the angle of the jaw, or it may be located in the upper part of the neck. The patient rarely has any complaint other than facial dis-

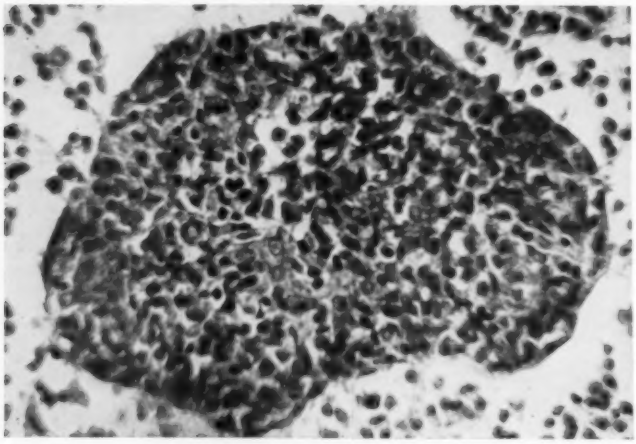

Fig. 5. Benign lymphoepithelial lesion, showing epimyoepithelial island.

figurement. The tumor is slow growing and is usually present months or even years before the patient seeks medical advice. Eighty per cent of the tumors occur in the 40 to 70 year age group.[7] Less than 10 per cent are under 40. The youngest recorded case in the literature is a two-and-a-half year old child.. Males are affected five times more than females. Bilateral tumors are not common; only 11 cases have been reported.[14]

To palpation, the tumor is a smooth, round or oval mass which is usually moveable and is moderately firm to cystic in consistency.

When the tumor presents in the neck, it is located along the anterior border of the sternomastoid muscle. In this location, it is in contact with the posterior border of the submaxillary gland. This finding has led some authors to conclude that the tumor arises from the submaxillary gland. Martin and Ehrlich[22] believe that this is an error due to failure to realize that a tumor arising from the tail of the parotid will come in contact with the submaxillary gland. All of their 25 cases arose or were connected with the parotid alone.

DIAGNOSIS.

A clinical diagnosis of this tumor is rarely made before histological examination. It is usually diagnosed as a mixed tumor of the parotid or as a branchiogenic cyst when it presents in the neck.

Twenty-five cases of papillary cystadenoma lymphomatosum were found in the pathology files of the University Hospital and an additional six cases at Bellevue Hospital. Twenty-eight cases were males, and three were females. All patients were between 40 and 60 years old. In one patient both parotid glands were involved.

DIFFERENTIAL DIAGNOSIS.

The tumor must be distinguished from: *1.* mixed tumors of the parotid; *2.* malignancies; *3.* branchiogenic cysts; *4.* lymphomas; *5.* leukemia; *6.* metastatic carcinoma from the undiscovered primary in the oral or pharyngeal cavities; and *7.* Mikulicz's disease. The means available for diagnosis are sialography and aspiration biopsy.

Sialography in Warthin's tumor shows displacement of the duct system when the tumor is within the parotid, and no change in the ductual pattern when it is extracapsular,[4] thus the sialogram does not distinguish it from other encapsulated lesions; however, in Mikulicz's disease, where the pathology is in the ductal system, sialography is helpful in diagnosis, especially when distortion and sialectasis can be demonstrated.

Aspiration biopsy may be used to establish a diagnosis prior to surgery. If the aspirated material contains the papillary layer, the diagnosis is not difficult; however, if only lymphoid tissue is obtained in the aspiration, the diagnosis cannot be made. Martin and Ehrlich[22] reported 12 positive biopsies in 18 cases in which they had done aspiration biopsies. Because there is some danger of spilling cells from a mixed tumor during an aspiration biopsy, a frozen section at the time of surgery is preferred.

Papillary cystadenoma lymphomatosum should be distinguished from "the benign lymphoepithelial lesion"[13] or Mikulicz's disease. In 1888, Mikulicz[23] described a case of a young man with enlargement of the lacrymal and salivary glands. Mikulicz insisted that the lacrymal gland involvement was an essential part of the condition. Morgan and Castleman[25] have shown that the lesion may not involve the lacrymal gland, but may be limited to one or two salivary glands.

Mikulicz's disease occurs predominantly in women in the fifth and sixth decades. Eighty-three per cent of Morgan and Castleman's cases were females.

Histologically, the tumor is composed of lymphoid tissue in which are found epimyoepithelial islands. The epimyoepithelial islands are produced by intraductal proliferation of epithelial and myoepithelial cells. The lymphoid stroma appears as an infiltrate which replaces the normal gland structure. Germinal centers are few.

The etiology and pathogenesis of the disease are obscure. Most investigators believe it is a reactive or inflammatory disease. Bauer[2] is convinced that it is a neoplasm and bases this conclusion on the active new growth of the epithelial cells in recurrences.

Morgan[24] has suggested that Mikulicz's disease is related to Sjogren's syndrome (keratoconjunctivitis sicca, bucco-pharyngo-laryngitis sicca, swelling of the salivary gland and polyarthritis) and that the histological picture is similar in both diseases.

Warthin's tumor and Mikulicz's disease have several features which may be contrasted (see Table II).

TREATMENT.

Treatment of papillary cystadenoma lymphomatosum is surgical excision. Since the majority of tumors are found in the superficial portion of the gland, they can be removed without disturbing the facial nerve. When the lesion is

TABLE II.

Papillary Cystadenoma Lymphomatosum. Warthin's Tumor.	Benign Lymphoepithelial Lesion. Mikulicz's Disease.
1. Neoplastic.	1. Inflammatory, reactive, neoplastic?
2. Males predominant—5 to 1.	2. Females predominant—4 to 1.
3. Age—40 to 70.	3. Age—5th to 6th decade.
4. Parotid only.	4. Salivary and lachrymal glands.
5. No symptoms.	5. Dryness of mouth and pharynx.
6. Sialogram — displacement of ducts.	6. Distortion and sialectasis.
7. Aspiration biopsy—positive 2/3 of cases.	7. Not diagnostic.
8. Histology—papillary, epithelial layer. Lymphoid tissue with germinal centers.	8. Epi-myoepithelial islands. Lymphocytic infiltration.
9. Treatment—surgery.	9. Treatment—surgery and/or radiation.

multicentric or is located in the substance of the gland, the modern principles of parotid surgery should be followed. The facial nerve is located as it enters the posterior aspect of the parotid, and the entire superficial portion of the gland, with the tumor, is removed without injury to the facial or its branches. When the tumor is located in the deep portion of the gland, the facial nerve is gently retracted while the deep portion of the gland is dissected from the nerve and the surrounding structures. There is no justification for sacrifice of the facial nerve or its branches.

The prognosis of this tumor is good. There are no authentic cases of malignancy that have withstood critical analysis. Recurrences are less than 10 per cent and are due to incomplete removal. Radiation therapy has no effect on the tumor.

The treatment of Mikulicz's disease is either surgery or

radiation therapy. Godwin[13] advocates surgery followed by radiation. In bilateral cases after surgical excision of one side, he advocates radiation therapy for the opposite side, instead of surgical excision. The response to radiation is good and recurrences are less than in surgery.[26] There were seven cases of benign lymphoepithelial lesion (Mikulicz's disease) found in the pathology files at University and Bellevue Hospitals; five of these were females; two were males. All were treated surgically.

CONCLUSIONS.

1. Papillary cystadenoma lymphomatosum is the third common neoplasm of the parotid; it accounts for about five per cent of all parotid tumors.

2. It is a benign neoplasm composed of epithelial and lymphoid elements; its histogenesis, while not certain, probably is from salivary gland rests found in lymph nodes of the parotid region.

3. Clinically, it is indistinguishable from other benign, nontender parotid swellings. Positive diagnosis depends upon histological examination.

4. Treatment of papillary cystadenoma lymphomatosum is surgical. Radiation has no effect on the tumor.

5. Benign lymphoepithelial lesion, or Mikulicz's disease, is also composed of epithelial and lymphoid elements, but is a distinct clinical and pathological entity.

6. Treatment of Mikulicz's disease is surgery or radiation or a combination of both. The response to radiation is good and recurrences are few.

7. Sacrifice of the facial nerve is not justified in either Warthin's tumor or Mikulicz's disease.

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SOME OTOLARYNGOLOGICAL ASPECTS OF CEREBROVASCULAR DISEASE.*

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Cerebrovascular diseases constitute the nation's third ranking killer. It has been estimated that as many as 1,800,000 living Americans have suffered strokes, and that deaths due to such strokes total nearly 175,000 annually. Many strokes are preceded by transient warning episodes which may first be called to the attention of otolaryngologists. In particular, symptoms suggestive of inner ear disease may be due to cerebrovascular disease. Such disturbances may remain obscure unless thought of in the light of a cerebrovascular lesion. Numerous personal experiences with vascular complications prompted this review of the subject.

The principal types of cerebrovascular disease are: atherosclerotic occlusion with cerebral infarction, transient ischemia without infarction, intracranial hemorrhage, vascular malformations and developmental abnormalities, inflammatory disease of arteries, hypertensive encephalopathy and dural sinus and cerebral venous thrombosis.

The number and variety of neurologic symptoms and signs that may be encountered are almost unlimited and their recognition requires a knowledge of neurology. Recognition of impending strokes has become very important, in that medical measures such as the use of anticoagulants or surgical intervention may pervent a catastrophic outcome. These warning attacks usually last from two to ten minutes. Many attacks may occur over a period of weeks or months. The syndromes of impending stroke may manifest themselves from the territory of each of the major cerebral arteries as follows:

1. Middle cerebral artery: contralateral mono- or hemi-

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paresis, numbness, tingling, dysphasia, homonymous hemianopia or scintillating scotomata.

2. Anterior cerebral artery: weakness or numbness of the upper limb, confusion, psychotic manifestations and incontinence.

3. Posterior cerebral artery: homonymous hemianopia, scintillating scotomata, and if there is bilateral involvement, temporary or permanent blindness.

4. Internal carotid artery: contralateral weakness, numbness or dysphasia, transient blindness on the side of the occluded vessel and reduced pulsation of the common or internal carotid artery in the neck or inside the pharynx.

5. Vertebral-basilar arteries: dizziness, monoparesis, hemi- or quadriparesis, numbness involving both sides of the body, staggering, ataxia, diplopia, dysphagia, dysarthria, tinnitus, deafness, visual disturbances, temporary confusion or loss of memory and unconsciousness. Characteristically the complaints are bilateral in vertebral-basilar disease and unilateral in middle, anterior, and posterior cerebral and in internal carotid involvement.

CASE HISTORIES.

A brief report on a group of ten cases will serve to illustrate the symptomatology and the diagnostic procedures and findings in representative cases.

Case 1. W.D., 63, male, was admitted to Detroit Memorial Hospital because of hoarseness due to left vocal cord paralysis of several weeks' duration. Treated for two years for hypertension. Right carotid compression resulted in syncope. Carotid arteriograms showed complete occlusion of the left internal carotid artery just distal to its origin. Carotid artery exploration confirmed the total occlusion. The artery was ligated distal to the occlusion, and a left cervical sympathectomy was done. Long term anticoagulant therapy was instituted. The vocal cord paralysis was probably due to a coexistant infarction of the vagus nucleus in the medulla, resulting from vertebral basilar disease.

Case 2. E.P., 53, male, admitted with tinnitus and progressive left hearing impairment of seven years' duration. Two weeks previous to admission he had a sudden onset of dizziness, throbbing headaches and difficulty in moving the right leg. Right carotid artery compression resulted in blurred vision, dizziness and diplopia. Left carotid compression produced numbness in the right hand. Left carotid arteriogram showed arteriosclerotic changes within the proximal portion of the left internal carotid artery.

Case 3. A.T., 69, male. The day before admission he awoke with tinnitus on the left, occipital headache and dimness of vision in the left eye (right eye blind from trauma in childhood). Left carotid compression produced dimness of vision but no syncope. Bilateral carotid arteriograms showed arteriosclerotic placques in the proximal portion of both internal carotids, the left carotid being occluded.

Case 4. S.B., 62, female, admitted with headaches and right-sided tinnitus. Left carotid compression resulted in syncope. Right carotid angiogram showed arteriosclerotic changes in the right internal carotid artery just distal to the bifurcation and at the syphon. There was also anterior cerebral artery occlusion at its origin.

Case 5. E.D., 51, male, admitted with dizzy spells of eight months' duration, which were relieved by lying down, and parasthesias in the right arm. Bilateral compression produced dizziness. Arteriograms revealed a right carotid artery occlusion.

Case 6. J.L., 63, male. Three weeks previous to admission, patient had sudden onset of dizziness with nausea and vomiting and pulsating tinnitus in the right ear. The audiogram and caloric tests were normal. Left carotid compression produced syncope. Arteriograms revealed right carotid artery occlusion.

Case 7. M.F., 80, female, admitted with dizziness and bilateral tinnitus of two weeks' duration. On the morning of admission she developed generalized weakness, vomiting and speech disturbances. Left carotid compression resulted in syncope. Carotid arteriograms showed bilateral placques with occlusion of the right anterior cerebral artery.

Case 8. A.H., 67, male, admitted with dizziness of two months' duration. Left carotid compression slowed the pulse to 35. Right carotid compression produced asystole. Autopsy revealed vertebral artery occlusion with evidence of infarction.

Case 9. A.F., 71, female; left pounding tinnitus for two months and dizziness for a month before admission. Tinnitus relieved by carotid compression. The caloric test was normal. The audiogram showed a moderate degree of nerve-type hearing impairment bilaterally. Carotid compression produced syncope. Arteriograms showed almost total occlusion of the left carotid. A small placque was noted on the right carotid.

Case 10. J.W., 62, male, admitted with severe vertigo, and persistent left tinnitus of six months' duration. Audiograms show a bilateral symmetrical nerve type of hearing impairment. A weak caloric response was obtained on the left. Bilateral carotid compression produced syncope. EEG reported as showing a bi-temporal dysrhythmia (slowing), suggesting a mid-line disturbance, probably vascular. Right carotid and vertebral arteriograms showed a normal right carotid and a straightening and elongation of the basilar artery indicating arteriosclerosis but without obstruction. The vertebral arteries were normal.

The symptoms of the patients above described, although in part otological, are actually a result of cerebrovascular insufficiency. This insufficiency is frequently due to occlusive disease of the carotid vertebral-basilar system.

DISCUSSION.

The increased diagnostic use of carotid arteriography and routine examination of these arteries in autopsy examinations,

have shown that carotid artery occlusion exists much more often than was formerly believed. Advanced atherosclerosis, including complete obstruction of one or both of the carotid vessels, was found in 9.5 per cent of 432 consecutive routine autopsies in which the carotid arteries were deliberately studied.[2] Many recurring temporary neurologic episodes previously considered to be caused by "vasospasm" and the "little strokes" of Alvarez, are now believed to be due to carotid artery occlusion.[1] The site of involvement is usually located at the bifurcation of the common carotid artery or in the proximal portion of the internal carotid artery. Less commonly the common carotid is involved.

Three general clinical carotid syndromes are recognized:

1. The apoplectic type with a sudden onset of severe neurologic symptoms due to complete and rapid occlusion of the carotid artery. The findings may be a contralateral hemiplegia, visual disturbances on the affected side, aphasia and coma. It may be rapidly fatal, or the patient may survive with varying degrees of permanent neurologic sequelae. This type occurs in 35 per cent of patients with carotid artery occlusion.[6]

2. The episodic type, with transient recurrent episodes of fainting, dizziness, paresthesias, paresis, aphasia and visual disturbances. They may recur over a period of many months and often terminate in hemiplegia. This type is noted in about 40 per cent of patients.

3. The progressive type, exhibiting a slowly progressive course with headache, paresthesias, paresis, irritability, memory loss, depression and mental regression. This type occurs in about 25 per cent of the cases. The nature of the progression often mimics a brain tumor.

Once the possibility of a cerebrovascular lesion is considered, several diagnostic procedures may be carried out. They are: lumbar punctures, air studies, electroencephalography, carotid compression tests, ophthalmodynamometry, and angiography.

The carotid sinus reflex test can be carried out at the time of the initial examination. Digital compression of the carotid

bulb is applied carefully with the patient sitting upright. An assistant notes the pulse while the carotid bulb is first gently palpated and then gradually compressed. At the first sign of syncope or convulsive movements, the compression is released, and the patient is put in a supine position. This test has not proved dangerous in hundreds of cases, but it must be used cautiously. Usually, compression for 10 to 20 seconds is required before syncope occurs from the induced acute cerebral ischemia. An immediate onset of syncope, which is much less common (five seconds), usually indicates a "sensitive carotid sinus."

No abnormality is noted on compression or palpation of the carotid bifurcation in young healthy individuals; in others, one of three responses or various combinations of these may be obtained:

1. There may be an irritable carotid sinus and, on compression or palpation of the carotid sinus, there is produced a prompt asystole followed by syncope, often within five seconds. Loss of consciousness is abrupt without aura. There is no memory of the experience. The asystole is produced by the cardio-inhibitory vagal reflex which may be abolished with atropine.

2. Another response infrequently seen is a severe drop in blood pressure as a result of a vasodepressor reflex. There is question as to whether this is a carotid sinus effect or a reflex effect with vasodilation in the gastrointestinal and muscular vascular bed. Such vasodepressor effects, according to Gurdjian et al.[3,7] are seen in the patients undergoing venipuncture, observing blood or bleeding, witnessing an operation, etc. Usually the phenomenon cannot be repeated.

3. Syncope may occur without bradycardia or vasodepression. This third type of reaction has been called the cerebral form of carotid sinus irritability. Gurdjian[3,7] and his coworkers have found that this reaction is due to occlusive vascular disease involving the opposite carotid, the anterior cerebral or the basilar arteries. They conclude that this type of syncope is due to ischemia of the brain. A carotid sinus inhibitory reflex may, of course, be superimposed upon the

ischemic response. In the presence of occlusive carotid artery disease, collaterial circulation may exist to a degree which precludes syncope, but dizziness, malaise, contralateral numbness or weakness may occur. Contralateral convulsive movements are commonly seen, particularly in the arm. Syncope usually occurs just before the onset of the convulsive movements; these movements may then increase as the patient regains consciousness. Change in mental status, such as confusion, disorientation, agitation, and an appearance of fear followed by amnesia are common. Usually the patients are asked to count as the compression is applied. They are unable to continue with the onset of the ischemic effect, often before syncope begins.

Arteriography of the carotid and the vertebral systems may then be indicated. It is the most satisfactory method for diagnosing carotid artery occlusion. The contrast media must be injected low in the neck to examine properly the entire carotid system. Carotid angiography has occasionally been followed in the past by hemiplegia and visual disturbances, which were transient in the great majority of cases. These complications are much less common now due to improved contrast media. Arteriography has its limitations in that small blood vessels are not well outlined with present day techniques.

TREATMENT OF CAROTID OCCLUSION.

Anticoagulant drugs may have considerable value in the prevention of a thrombotic occlusion. Symptoms of intermittent transient attacks of vertigo, paresthesias and paresis may precede the formation of a massive thrombosis or the extension of a thrombus. The use of anti-coagulants in these cases may be of considerable temporary value. The use of drugs to counteract arterial vasopasm have not produced satisfactory results.[1]

Various types of surgical operations have been used. They include thromboendarterectomy (intimectomy), resection and external carotid anastomosis, resection of the involved portion of the artery with replacement by an arterial homologous

graft, and resection with replacement by prosthesis.[4,5] A concomitant sympathectomy may be done to increase the vascular supply to the head.

CONCLUSIONS.

1. A diagnosis of "stroke," "cerebral thrombosis," "cerebrovascular disease" and "embolism" may be related to ischemia of the brain, due to occlusive disease of the carotid-vertebral artery system.

2. Carotid-vertebral arterial occlusive disease may become manifest by the appearance of transient warning signs and symptoms, some of which are first called to the attention of otolaryngologists.

3. Recognition of these "warnings" are important, in that appropriate steps may be taken to prevent a catastrophic "stroke."

4. The carotid compression tests can be done at the initial examination to determine the adequacy of the carotid circulation.

5. This test should become a common diagnostic procedure, especially for differentiating obscure otological conditions.

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THE FIRST ONE HUNDRED CASES OF HEARING IMPROVEMENT IN STAPES MOBILIZATION—A LONG TERM REPORT.*†

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The first case of hearing improvement following mobilization of the fixed stapedial footplate by Rosen[1] occurred in April, 1952. Since then many patients with otosclerotic deafness have been operated upon by the indirect method of stapes mobilization, which consists of exerting pressure in a posterior direction on the neck of the stapes. The direct method of mobilization at the footplate itself and the technique of fenestration of the oval window were subsequently developed and reported by the same author.[2,3]

In our first statistical report of the results achieved by the indirect method of stapes mobilization,[4] read at the Fifty-Ninth Annual Meeting of the American Laryngological, Rhinological and Otological Society in March, 1955, one of the questions we asked was: "Will the hearing restored by this technique last?" Of 61 improved cases included in that report, eleven were then more than one year after mobilization, while two were over two years.

It seems appropriate at this time, almost seven years after the first mobilization, to examine the postoperative hearing data of the earliest 100 successful cases to determine:

1. How many of these patients have retained their maximum postoperative hearing improvement.

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2. How many showed partial regression in hearing from the best levels recorded postoperatively, but who still have significantly better hearing than they did preoperatively.

3. How many suffered complete regression of hearing to their preoperative thresholds, and when such regression occurred.

4. How many of the regressed cases were revised and with what results.

5. How many were revised in an effort to obtain still more improvement and with what results.

SELECTION OF CASES.

The 100 cases included in this follow-up had all been operated upon by the indirect method of mobilization of the fixed stapedial footplate by exerting pressure on the neck of the stapes, as reported by Rosen in 1953.[5] They are the earliest chronologically consecutive cases with adequate test data in which recent follow-up tests were available or could be obtained. Any early case where follow-up data was unobtainable was excluded from this study. Twenty-four cases among the early chronologically consecutive cases had to be excluded because recent follow-up data were unavailable for the following reasons: two patients deceased; 18 patients, present address unknown; four patients did not return for follow-up tests despite requests to do so.

The criterion for significant improvement was a gain in hearing, as noted by the speech reception threshold (SRT), of 15 db or better. Conversely, hearing was recorded as having regressed if the most recent test data showed the SRT to be worse by 15 or more db than the best SRT recorded postoperatively. Among the latter group, a case was considered to have regressed completely if the SRT was less than 15 db above the preoperative level; and partially regressed if the patient still had an SRT better by 15 db or more than the preoperative level. The mean error between SRT's and pure tone threshold averages at 500, 1,000 and 2,000 cps on the equipment used in the follow-up testing of all

patients in this series was 0.57 db, with a standard deviation of 4.94.

FINDINGS.

Of the 100 cases included in this study, 80 were found to have maintained their maximum improvement levels without regression or without further surgery. Ten of these submitted to further stapes surgery in the previously operated ear for the purpose of improving their hearing beyond the levels obtained on the first operation. At the time of the revisions, none of these cases had shown any regression. The

TABLE I.

Duration of Best Postoperative Thresholds in Non-regressed Cases.

Duration	No. of Cases	
1 to 6 months	0	
7 to 12 months	6	*
13 to 18 months	2	
19 to 23 months	0	
2 to 3 years	2	
3 to 4 years	29	
4 to 5 years	35	
5 to 6 years	5	
Over 6 years	1	
Total	80	

*These ten cases were revised to increase their hearing still further as just stated.

remaining 20 patients showed regression in hearing; 16 completely and four, partially. These data are summarized in Table I, which also shows the length of time from the date of surgery to the most recent hearing test.

From Table II we see that two of the improved cases regressed completely within the first six months after operation; two cases regressed within seven to 12 months postoperatively; three cases between 13 and 18 months; two cases between 19 and 23 months; four cases between two and three years and three cases between three and four years postoperatively.

Of the 16 cases of complete regression, nine were revised,

with seven once again enjoying and maintaining significantly improved hearing.

Of the four cases which showed partial regressions from the best levels reached postoperatively, one had maintained the maximum improvement for almost four-and-a-half years, another for almost four years, a third for almost three-and-a-

TABLE II.

REGRESSED CASES.

Duration of Best Postoperative Thresholds Before Regressions Occurred.

Duration	No. of Cases Completely Regressed	No. of Cases Partially Regressed
1 to 6 months	2	
7 to 12 months	2	
13 to 18 months	3	
19 to 23 months	2	1
2 to 3 years	4	
3 to 4 years	3	2
4 to 5 years	0	1
Total	16*	4

*Six of the 16 had originally achieved only a 15 db improvement in hearing, sufficient gain, though small, to be included in the improved cases. If, however, they were found to have even 5 db less hearing on subsequent tests, they were considered to have regressed completely. Of all the regressed cases, none showed hearing which was worse than their preoperative hearing.

TABLE III.

PARTIAL REGRESSIONS.

Case No.	Preop. Threshold	Best P.O. Threshold	Duration of Best P.O. Threshold	Present Threshold	Total P.O. Period
1.	50 db	15 db	53 months	30 db	58 months
2.	55 db	25 db	47 months	40 db	52 months
3.	50 db	15 db	41 months	30 db	50 months
4.	60 db	25 db	23 months	40 db	56 months

half years, and the fourth for about two years. In the Table which follows, note that Cases Nos. 1 and 3 still hear at a threshold level of 30 db, while No. 4's threshold of 40 db is still 20 db better than before the surgery four years and eight months previous to his most recent test.

Ten of the patients who were considered to have had significant improvement in hearing following the first stapes mobilization were dissatisfied with their postoperative hear-

ing levels and were reoperated in an attempt to improve their hearing further. Following the first operation, the threshold of one of these patients had been improved from 55 db to 40 db. Twelve months later she was reoperated by the direct method of footplate mobilization. (The crura were found to have been fractured at the initial operation.) The hearing improved after the second operation to the 15 db level by

TABLE IV.

Summary of the Present Status of the First 100 Cases Improved by Stapes Mobilization (Rosen).

	No. of Cases
1. Maintained Full Improvement	79
2. Successfully Revised Following Complete Regression to Preoperative Thresholds	7
3. Partially Regressed but Still Significantly Improved Over Their Preoperative Levels	4
Total with Significantly Improved Hearing at Most Recent Hearing Test	90
4. Completely Regressed to Preoperative Threshold and Unimproved by Attempted Revision	2
5. Completely Regressed, No Attempts at Revision	7
6. Dropped to Original Preoperative Level by Attempted Revision to Improve Hearing Further	1
	10
Total Cases	100

speech reception threshold, which has been maintained for over three-and-a-half years.

Another of these patients who had also improved only from a preoperative threshold of 55 db to a postoperative 40 db, was revised 12 months after the first operation. A fenestration of the oval window was performed, and the patient now has a remarkable improvement to her present threshold of 10 db, three-and-a-half years following footplate fenestration.

A third case revised in an attempt to increase the gain in hearing 13 months after the original operation had brought the hearing from a preoperative threshold of 60 db to 45 db, returned to the 60 db level following the revision attempt.

The remaining seven cases of the ten revised for further

improvement did not gain more hearing, but remained at the postoperative threshold achieved at the first operation. They are, therefore, included among the cases which maintained full improvement by stapes mobilization at the neck.

Table IV summarizes the present status of the first 100 cases included in this report.

SUMMARY.

This report contains a follow-up study of the present hearing of the first 100 successful cases of stapes mobilization. Eighty-three of these patients have maintained significantly improved hearing for from three to seven years. Following successful revision of seven of the regressed cases, 90 of the original 100 successful cases today enjoy significantly improved hearing.

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LATE HEARING RESULTS IN MOBILIZATION SURGERY.*†

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The destiny of the various techniques for securing stapes mobility may not be clearly projected, but time is beginning to furnish some clues concerning the practicability of continuing to attack the stapediovestibular junction as the logical approach to solving the problem of otosclerotic ankylosis. Currently enthusiasm seems to prevail for the improvement in results achieved over the past five years, and for the promise of new developments in surgical technology that are continuing to evolve from experimentation.

At the outset it was generally conceded that the obstacles to obtaining stapes mobilization would not be too difficult to overcome. Subsequent events seem to have confirmed this prediction. It is probably conservative to estimate that 80 to 90 per cent of otosclerotically fixed stapes may be at least partially mobilized by the present methods of approaching the footplate directly; however, regressions continue to occur in proportionately increasing numbers to detract from the gains made in the rate of mobilization.

According to gross and microscopic observation, it is apparent that the disposition and the extent of the otosclerotic process in the stapediovestibular joint is distributed in such peculiar patterns in the population so as not only to defeat efforts to mobilize some, but also to limit the numbers of long term results. A study of early experiences reveals some interesting facts:

The first 100 immediately successful results obtained three

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to five years ago developed out of 206 attempts to mobilize the stapes in patients whose hearing loss occurred from stapediovestibular otosclerosis. This represents a temporary success rate of 49 per cent, and all but four of these were mobilized by engaging a pick in the head of the stapes, as previously described in 1955.[1] The four exceptions were mobilized by the pulsating technique applied to the head and neck of the stapes, reported by Rosen.[2] All but 17 patients have had audiograms during the past six months. The rest have had audiograms during the past year.

SUCCESSES.

Among the first 100 successes, 54 have maintained their gain of 15 db or more in the speech frequencies of 500, 1,000 and 2,000 cycles per second. Thirty-four of these have

TABLE I.

At least 15 db improvement	54	
Hearing better than 30 db	34	(16)*
Not better than 30 db	20	(2)*

*(16 and 2)—Closure of the air-bone gap.

hearing of better than average 30 db including 16 which have closure of the air-bone gap. Only two of the remaining 20 also have closure of the air-bone gap. Closure of the air-bone gap is defined as a difference of ten db or less between the preoperative bone conduction threshold and the postoperative air conduction threshold (see Table I).

REGRESSIONS.

Regression is defined as a decrease of hearing to any threshold below all of the categories of success. In other words, when an initial success subsequently drops to any level below the "15 db gain," "better than 30 db," and/or "air-bone gap closure" category, it is considered a regression. Among the first 100 successful ears, 46 regressions subsequently occurred as follows (see Table II):

Nineteen of these 46 regressions have been reoperated and

six have subsequently regressed again. At least two of the regressions occurred because of ischemic necrosis of the lenticular process which developed from circulatory trauma of the pick on the capitulum. It is believed that most of the other regressions occurred as the result of reankyloses due to otosclerosis or fibrosis of the footplate. Two patients have since had successful fenestration operations—one after the initial attempt to mobilize the stapes and one after two attempts to secure mobilization. The low incidence of fenestrations is due to the fact that in the early stages of mobilization

TABLE II.

a. 28 regressed before one year after surgery—most of them within three months.	
b. 5 regressed between one and two years after surgery.	
c. 11 regressed between two and three years after surgery.	
d. 2 regressed between three and four years after surgery.	

surgery most of the patients selected were not suitable for fenestration surgery. The others have not been reoperated for various reasons classified under the notation "inadvisable to operate again"—usually complete displacement by otosclerosis.

COMPLICATIONS.

Some complications occurred among the maintained successes as well as among the regressions. There were two instances of purulent otitis media, one which responded promptly to treatment with recovery of the hearing gain, and one which eventually resolved without hearing improvement. Another patient developed serous labyrinthitis—unusual because a severe hearing loss ensued which after intense therapy regained the initial improvement. The details have been published elsewhere.[1] Two patients whose hearing improvement subsequently regressed continued to complain of chorda tympani injury.

COMMENT.

It should be emphasized that the technique used in all but

four of these operations was the engagement of the pick on the capitulum of the stapes. With experience the results have improved. A total of 707 operations were performed by this technique during the period 1954 through 1957. Sixty-five per cent of these were initially successful. As of Dec. 31, 1958, 58 per cent, or a little over one-half of the initially successful gains have been maintained. The regression rate is 42 per cent.

Comparing these results with 179 operations performed during the past two years with chisels applied directly to the periphery of the footplate, 83 per cent were initially successful. As of Dec. 31, 1958, 62 per cent of the initially successful gains have been maintained. The regression rate is 38 per cent.

TABLE III.

Summary of Results.

	6 Weeks	3-5 Yrs.	Regressions
At least 15 db improvement	100	54	46
Hearing better than 30 db	63 (23)*	34 (16)*	29 (7)
Hearing not better than 30 db	37 (2)*	20 (2)*	17 (0)

( )*—Closure of air-bone gap.

Despite the initial superiority of the chisel-footplate technique over the pick-capitular technique regressions continue to undermine the sustained results. As such evidence arises, gradual shifts to variations and modifications of the operation are made. The current trend is toward artificial struts[3] and footplate substitution techniques,[4] which may reduce the incidence of regressions and, therefore, assure a larger number of sustained improvements.

SUMMARY.

Three to five years after stapes mobilization by the pick-capitulum technique, 54 of 100 initially successful operations are still successful according to the criteria set forth above. Forty-six have regressed, 28 of these before one year post-operatively.

Thirty-four of the 54 sustained improvements have a hearing threshold of better than 30 db, and 18 of the 54 resulted in a closure of the air-bone gap (see Table III).

The chisel-footplate technique is superior to the pick-capitulum method, but regressions continue to take a proportionate toll of sustained results. The technically more difficult uses of artificial struts and footplate substitutes which are being phased in with our past experiences may offer better prospects of permanency.

ACKNOWLEDGMENT.

The indispensable statistical evaluation provided by Dr. James L. Shapley, Ph.D., and Patricia Iles, B.A., is gratefully acknowledged.

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TRANSTYMPANIC VESTIBULOTOMY FOR MENIERE'S DISEASE.*†

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Transtympanic labyrinthotomy is the simplest of the surgical procedures for Meniere's disease available today.[1,2] The results reported have been good, although some patients have had recurrence of vertigo.[2] A new technique is presented that should produce uniformly good results without recurrences.

Surgical treatment of Meniere's disease is indicated when medical management fails to control the attacks. Surgery is also indicated in certain patients whose anxiety over the possibility of another attack renders them psychologically incapacitated. It is to be sure that patients deserve a careful history and examination, as well as a trial on an appropriate medical regimen before subjecting them to labyrinthotomy.

TECHNIQUE.

The operation presented represents an attempt to avoid the failures occasionally experienced with earlier methods.[2,3,4,5] The objective is destruction of the entire statico-dynamic function of the labyrinth. The position of the macula utriculi and the macula sacculi in relationship to the round window and the stapes is clearly seen in Fig. 1. By removing the stapes *and* the promontory between the round and oval windows one can obtain direct access to the saccule, utricle, common crus, non-ampullated end of the horizontal semicircular canal, and the ampullated end of the posterior semicircular canal. In this way the ultimate loss of all vestibular function can be assured.

General anesthesia is employed to avoid vertigo, nausea,

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and vomiting during the operation. Hemostasis and supplementary anesthesia are obtained by infiltrating approximately 1 cc. of a mixture composed of equal parts of procaine 1 per cent and epinephrine 1:1000. The incision is made and the skin flap elevated in the usual manner for transtympanic surgery.

The incudostapedial joint is disarticulated and the stapedius tendon divided. The stapes is gently rocked with a rotary

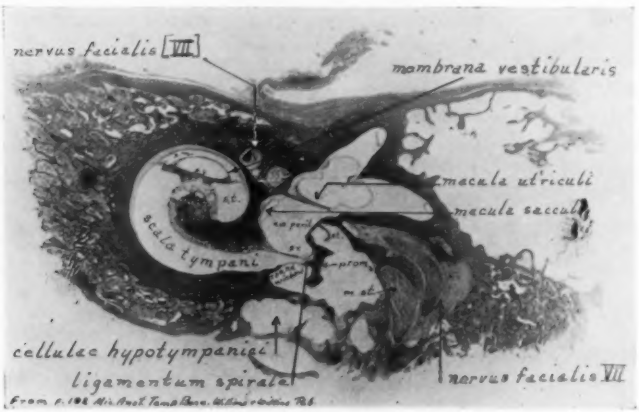

Fig. 1. Photomicrograph of a vertical section cut in the plane of the long axis of the petrosa. St—stapes. Modified by D. Wolff and reproduced with permission from "Microscopic Anatomy of the Temporal Bone," Wolff, Bellucci and Eggston, The Williams & Wilkins Company, Baltimore, Md.

motion to loosen it, so that it can be removed intact by grasping the capitulum with middle ear forceps. A small curette is then introduced into the round window, and the bone between the two windows is carefully removed (see Fig. 2). The contents of the vestibule are removed by *gently* curetting the medial wall and scrubbing it with a cotton-tipped applicator. Vigorous curettage could result in a cerebrospinal fluid leak through the cribiform area leading to the internal auditory meatus and should be avoided. The vestibule is lightly packed with gelfoam to promote organization of a firm pro-

tective scar. The drum and flap are replaced. An antibiotic is administered for the first five days after operation.

RESULTS.

This is a new, but clinically promising technique. Only three patients have been operated upon in the manner described. All had a long history of recurrent attacks of vertigo

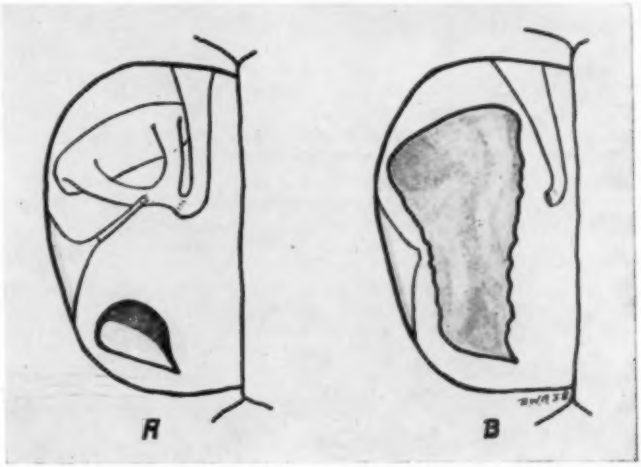

Fig. 2. A. Diagrammatic representation of the operative field. B. Stapes has been removed and the round window connected with the oval window by removing the intervening bone.

with nausea and vomiting, plus the usual tinnitus and progressive unilateral loss of hearing. All had an ample trial on medical treatment, and all failed to respond. In each instance there has been relief of vertigo and loss of caloric response as well as total loss of hearing in the ear subjected to surgery. Two patients were relieved of their tinnitus, but the other patient still complains of roaring in her ear. Convalescence has not been materially different from other types of labyrinthotomy.

SUMMARY.

A transtympanic technique that insures the destruction of the vestibular end-organs has been presented. One need not fear the unfortunate complication of facial parlaysis that has occasionally followed attempts to destroy labyrinthine function by injection of alcohol or electrocoagulation.[3] The operation described should eliminate the failures occasionally encountered with previously described operations. Experience with more cases will be necessary before final appraisal of this procedure is possible.

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NEURILEMMOMA OF THE FACIAL NERVE.*

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Neurilemmoma of the facial nerve is not a common condition. In a recent article in which he reported a case, Sarkar[1] stated that he had found 32 cases in the literature and documented them; his case made a total of 33. In most of the cases the primary symptom was a facial paralysis and the presenting sign a mass in the external auditory canal often diagnosed as a polyp. In many cases the erroneous diagnosis of Bell's palsy had been made and Kettel[2] reports such a case.

It is our purpose here to report four additional cases of neurilemmoma of the facial nerve. The first is not extraordinary, in that the presenting signs were a mass in the external auditory canal and a complete facial paralysis that had been present for some years. No definite diagnosis was made before operation.

The second case had been diagnosed as Bell's palsy by a neurologist, and the patient was referred to one of us (T.E.W.) for decompression of the nerve. Examination of the ear revealed an intact drum with a tumor mass occupying the posterior part of the middle ear. X-rays were not revealing, and the diagnosis of neurinoma of the facial nerve was made and confirmed at operation.

The third and fourth cases are of special interest, in that they both had intracranial extension of the neurilemmoma which arose in the horizontal portion of the nerve. They both were seen by one of us (L.T.F.) because of the signs of intracranial pathology. In one the tumor could be seen in

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the middle ear behind an intact drum. In the other there was no evidence of intratympanic pathology.

Case 1. M.D., female, age 35, was first seen in April, 1948, complaining of "trouble with the left ear and paralysis of the left side of the face." The trouble had started with tinnitus in the left ear in March, 1938. Eustachian tube inflations and tonsillectomy were performed with no effect on the tinnitus. In the Spring of 1939, some loss of facial movement was first noticed, and paralysis gradually became complete. The patient was seen at the Mayo Clinic in 1940 and an exploratory operation on the left ear was suggested but was not performed. In November, 1947, she experienced dizzy spells which were accompanied by nausea and vomiting. These spells had continued. There was no hearing in the left ear, and she had had no pain, headache nor change in taste.

Examination in April, 1948, revealed a complete left facial paralysis. In the left external auditory canal was a large red mass which was covered with skin and appeared attached both to the floor and to the roof of the canal. It was not possible to see past the mass, nor to examine the drum. A biopsy of this mass was not done, but it was felt that it must be removed by surgery. There was no hearing in the left ear.

At operation, a tumor mass was found eroding the posterior bony canal wall and filling the mastoid cavity. This was of a soft consistency, yellowish in color and bled fairly easily. The posterior fossa dura was exposed by the tumor which also filled the middle ear. The horizontal canal was eroded. The mass seemed to arise from the facial nerve both ends of which, superiorly close to the geniculate ganglion and inferiorly at the stylomastoid foramen, could be identified. The tumor was removed, and a graft, taken from the auriculotemporal nerve, was used. The patient did well postoperatively, except that there was no return of facial function.

She returned in March, 1949, complaining of continuing dizzy spells which were disabling and at that time was re-admitted and electro-coagulation of the left labyrinth was performed. Since then she has had no further trouble except for a minimal discharge from the cavity.

Case 2. B.R., female, 46, was first seen in September, 1950. This patient had been seen by a neurologist some seven or eight years previously complaining of a complete facial paralysis. This had been diagnosed as Bell's palsy, and she was told that nothing could be done about it. There was no recovery of function, and there was complete atrophy of the muscles on the right side of her face. She had had no pain and no difficulty with eating during this period, and the only real difficulty was epiphora of the right eye.

Examination of the right ear revealed a smooth swelling of the posterior half of the drum. The pars tensa moved freely over a mass in the middle ear. This mass when palpated with a cotton tipped applicator had the consistency of rubber. Testing for taste revealed a definite hypoactivity on the right side of the tongue. The hearing was not impaired. The diagnosis of neurofibroma of the facial nerve was made.

In April, 1951, an operation was performed to remove the neurilemmoma. A tumor was seen arising from the facial nerve and protruding into the antrum. It extended from 2 or 3 mm. above the stylomastoid foramen to just below the geniculate ganglion. There was no erosion of the bony labyrinth nor of the ossicles. Both ends of the nerve were found somewhat edematous and frayed, were freshened, and a graft taken from the auricular nerve approximately 20 to 25 mm. in length was inserted between the two ends. Healing was uneventful, and the

patient made a good recovery. There has been no improvement of the facial paralysis, and at a later date a fascial sling was done to improve the resting appearance of the face. The postoperative hearing shows a high tone loss above 2000 cycles.

Case 3. P.R., a white male, age 48, resident of Indiana, was seen on April 18, 1953. In 1940 he began to develop a peripheral facial paralysis which came on gradually and first involved the superior portion of the face. There was inability to blink and a smoothing out of the forehead. Eventually the paralysis became complete. In 1942 he was seen at the Mayo Clinic, but nothing of significance was found except for the right VIIth nerve palsy. The Department of Otolaryngology reported "negative" studies and there was no Vth nerve involvement. The presumptive etiology was pressure neuritis due to the patient's long established habit of sleeping with the right shoulder wedged into the right side of his face. A change of sleeping posture was recommended. He carried on his work as an automobile salesman and taxi driver without difficulty except for gradual loss of hearing in the right ear, which began in 1950 and was complete by 1952.

In December, 1952, while applying warm compresses to the exposed right eye, he was conscious of "whirling spots of bright colors" and that night during sleep he had a generalized convulsion. When he regained consciousness he was in an oxygen tent in a local hospital. Since that time, in spite of anticonvulsive medication, he had had five other convulsions, and during the last attack his left shoulder was dislocated. In January, 1953, while talking to a client he suddenly got up without any reason and left the client. The next thing he remembered was being in his car driving home. He had an uncontrollable desire to void, was incontinent of urine, and arrived home with wet clothes but no other reasonable excuse for being there. His wife volunteered that for several months he had been moody, irritable, careless in business and in dress, and uninterested in his home.

On examination he had no pressure signs and no Vth nerve involvement. There was an obviously long standing VIIth nerve paralysis on the right with eversion of the lower lid and pronounced sagging of the right face. There were no significant motor, sensory, or reflex changes, and no evidences of cerebellar dysfunction. He had several small cafe-au-lait spots on his back but no palpable neuromata. Audiometer test showed "slight remnants" of hearing in the right ear with normal hearing on the left. There was no reaction to caloric stimulation on the right except slight vertigo after four minutes of 68° water. Visual fields were normal. The EEG was interpreted as mixed fast and slow dysrhythmia, nonfocal, consistent with convulsive disorder. Radioactive isotrope localization was said to indicate a right cerebello-pontine angle tumor; however, X-rays of the skull showed a slight displacement of the pineal to the left and a thin curvilinear calcification extending up into the middle fossa, suggesting a large globular mass in this area. Until the X-rays were seen, in spite of the absence of Vth nerve involvement, an angle tumor was suspected. The films, however, raised the possibility of two lesions, so angiography was done. The right middle cerebral artery was displaced anteriorly, superiorly, and medially, so the middle fossa was explored on April 23, 1953.

The temporal bone was so thin that it was fractured with a periosteal elevator. A low flap was reflected. The very tight dura was controlled by ventricle puncture and release of spinal fluid. The sylvian fissure was found pushed upward at least three to four cms. A very thin layer of temporal cortex covered a tennis ball-size tumor of firm rubbery consistency. The interior of the tumor was yellowish in color with an occasional small cyst. Around the periphery of the tumor were several

areas of encapsulated yellow fluid in the arachnoid such as is seen over an VIIIth nerve tumor. With intracapsular enucleation the tumor was gradually collapsed down to a point of firm attachment along the mid-portion of the petrous bone. The medial margin of the tentorium was split. There was no evidence of tumor in the cerebello-pontine angle, so the dura around the point of attachment was sectioned, the tumor lifted out of a cavity which was thought to be the inner ear. With a chisel the bone around the edge of the area of tumor extension was removed and the site covered with gelfoam. The dural flap was resutured, no decompression being done. The patient had an uneventful postoperative course and was discharged. The tumor weighed 25 grams. The sections were reported as follows:

"Microscopic pathology—Section shows a tumor formed by intermingled bundles of fusiform cells. Verocays bodies are present. There are a large number of "foam cells" in the tumor. The underlying bone shows fibrosis of the marrow cavities and invasion by the tumor. No mitotic figures are seen."

This patient was discharged with diagnosis of tumor, verified, neurilemmoma, right middle fossa, VIIth or (?) VIIIth nerve. He continued to have an occasional convulsion, always nocturnal, but he takes only one grain of phenobarbital daily. He still has normal facial sensation and a deaf right ear, but no other abnormal neurological findings, except for the unchanged facial paralysis. He works regularly and feels well.

Except for an occasional follow-up note, this case history reposed quietly in the file until May, 1958, when Case 4, G.A.L., also a white male from Indiana, age 44, was admitted to Barnes Hospital. He was an insurance agent, and his history was a close parallel. He served in the Navy during World War II, was exposed to the noise of five inch guns and occasionally was temporarily deafened by this noise. In 1946, after discharge, he gradually developed a weakness of the right side of his face, and in 1947 went to the Mayo Clinic. He had a right facial paresis with decreased taste on the right anterior portion of his tongue, decreased hearing in the right ear, and no other abnormal neurologic findings. X-rays of his skull were negative. His condition was unchanged until 1950, when he was struck over the right side of his face with a baseball bat. His jaw was fractured, the cornea was lacerated, and this produced permanent visual impairment. In 1953 he had several dizzy spells, and again returned to the Mayo Clinic. There had been no apparent progression, and a diagnosis of angle lesion could not be made, so he was again sent home. There was no recurrence of dizziness, and he continued to work regularly until nine days prior to admission, when he had a nocturnal convulsion with incontinence. This was followed by a short period of combative behavior, and he was hospitalized. Spinal puncture showed increased pressure and protein, so he was transferred to Barnes Hospital. Neurological examination showed a dilated and irregular right pupil with a corneal scar (the result of an old injury), a complete long standing peripheral facial paralysis on the right, and a deaf right ear. The discs were normal and there were no other abnormal findings. Audiometry showed a totally deaf right ear, but caloric tests showed reaction on both sides. A mass was seen in the middle ear bulging against the posterior edge of the tympanic membrane which moved freely over it. Spinal puncture showed clear fluid with pressure of 190 mms. of water, and total protein of 143 mgms. per cent. E.E.G. was reported as follows:

"Record establishes convulsive character of past seizures we believe, but contribute little to localization of disorder; however, random slow spikes which appear, suggest organic etiology."

X-rays of the petrous bone and of the skull were reported as negative.

It was the consensus of opinion that this man had a VIIth nerve tumor which had eroded through the bone and extended into the middle fossa. Ventriculography was done on May 8, 1958, the ventricles being of normal size but displaced ½ cm. to the left. The anterior portion of the temporal horn was elevated, there was curvilinear collection of air beneath the temporal horn which was interpreted as air over the tumor arising from the floor of the middle fossa.

Immediate craniotomy was carried out. A low flap was reflected, the pressure being controlled by ventricle and spinal fluid removal, and a large smooth tumor, easily separated from the brain, was removed from the middle fossa. It was yellowish in color and contained a few cysts. It was firmly attached to about the midportion of the petrous portion of the temporal bone. The dura was split around the point of attachment and some adjacent dura which was invaded by tumor was removed, and additional tumor curetted out of the cavity which was thought to be the middle ear. For radiographic identification, a clip was placed in the bone opening and the wound closed.

Except for several convulsive seizures in the immediate postoperative period, his course was satisfactory. He was discharged on May 21, 1958. The tumor weighed approximately 10 grams and was reported as neurilemmoma of typical appearance.

The patient did well and was able to resume the major part of his regular duties. On July 15, 1958, using an endaural approach, the mastoid was opened. In the antrum, tumor could be seen extending from the middle ear. The tumor filled the middle ear, and the drum, malleus, and a small remnant of the incus were removed. No remnant of facial nerve could be seen. Just anterior to the usual location of the geniculate ganglion, a large hole in the bone contained tumor. When this tumor was removed, the silver clip previously placed there, was found to be attached to it. All the tumor was removed from the middle ear and the mastoid. Oxycel was packed into the dehiscence in the middle fossa and the rest of the cavity was packed with iodoform gauze. It was our opinion that this tumor had arisen from the facial nerve, and that the entire nerve had been replaced by tumor in its intratympanic course. Sections of the tumor were identical with those of the intracranial portion.

Following this procedure, there was cerebro-spinal otorrhea, so the patient was placed on antibiotics. In spite of some misgivings, he was discharged on the eleventh postoperative day to the care of a competent otolaryngologist for dressings and supervision.

Exactly one month later he was re-admitted to Barnes Hospital with fever, stiff neck, and 200 cells, 90 per cent polymorphonuclear leucocytes in his spinal fluid. He was put on intensive antibiotic coverage, and spinal fluid cultures were negative. When the packing gauze was removed from the ear, the drainage stopped; but he became drowsy, so X-rays were made. The films showed a large spontaneous pneumocephalus with a fluid level, so on Sept. 6, 1958, the bone flap was again elevated. About 50 cc. of air and 40 cc. of fluid were aspirated from a cavity in the temporal lobe. The cortex over this cavity was only a few mms. in thickness and when it was opened there was a point of adherence to the bone in the midportion of the petrous bone. The bone edge was freed, and an attempt was made to mobilize and suture the dura over this opening. This was impossible, so the bone opening was occluded with crushed temporal muscle, a piece of temporal fascia was incised and sutured to the dura over the muscle, and the wound was closed. His postoperative recovery was prompt and smooth with no further drainage. There was X-ray evidence of clearing of the pneumocephalus. The tissue removed was reported as focal fibrosis with no evidence of tumor. The

patient was discharged from the hospital and was seen in the office recently. He had resumed his former activities, and he was feeling quite well. He is still taking anticonvulsant medication.

The first case of the neurinoma of the facial nerve was reported by Schmid[3] in 1930. This was a 16-year-old girl who had a long standing facial paralysis, and a tumor mass on the posterior wall of the external auditory canal. Mastoid exploration revealed a cavity the size of a bean which was filled with granulation like tumor masses. The facial nerve was exposed in the descending portion at the bottom of the cavity and the pathological diagnosis was neurinoma arising from the sheath of the facial nerve. In 1931 Schroder[4] reported the case of a 25-year-old male who had had a facial paralysis for eight years with chronic purulent otitis media for four years. He had had two mastoid operations, and at the second operation the tissue removed was found to be neurinoma. At the third operation, a large tumor mass filling the middle ear and mastoid cavity was found and removed. An extension of the tumor into the middle fossa was not removed, but the patient was given X-ray treatment. One year later a small fistulous opening was injected with lipiodol, and the fistula was found to extend into the frontal lobe of the brain. The deafness and facial paralysis persisted.

Grossman and Leidler in 1932[5] reported a case which was later reported in detail by Altmann[6] with three other cases from the University Clinic in Vienna. This patient had had facial paralysis for 18 months, the external auditory canal was filled with polyps, there was conductive deafness with normal caloric reaction. Biopsy was reported as leiomyoma, and the patient was treated with radium. Six years later, the face was paralyzed and the patient was totally deaf. Operation disclosed a solid tumor filling the middle ear and the mastoid antrum. This tumor was removed and the sections were diagnosed as neurinoma. The patient recovered except for persistent facial.

In 1935, Altmann gave the first comprehensive report dealing with these tumors, and said that while such cases were rare the symptomatology was so clear cut that they could and should be diagnosed clinically. He reviewed the cases previously reported and gave detailed records of four addi-

tional cases, one being the patient previously reported by Grossman and Liedler. From these cases he formulated the following symptom-complex: The first symptom is always facial paralysis. It may come on suddenly, but usually is gradual in its development and may progress in a step-like fashion. Associated with the paralysis there is usually disturbance in taste, but if the tumor originates at a point distal to the chorda tympani taste may be intact. When the ear is examined a "polypous tumor" is usually found which obstructs either partially or completely the auditory canal, and it seems to have arisen from the posterior wall of the canal. Hearing is usually normal in the early stages, but later becomes impaired, either from external canal obstruction or by extension of the tumor into the middle ear. If the tumor in the middle ear erodes through the drum, infection develops, and this long standing drainage may complicate the symptomatology. He felt that irradiation of these tumors was useless, and advocated surgery as the only method of treatment; however, he felt that surgery was dangerous and to be undertaken only in the face of progression of symptoms. He stressed the fact that tumor removal did not alter the facial paralysis.

In a second paper in 1937, he reported an additional case and again reviewed the clinical syndrome. Altmann[7] advocated preliminary biopsy in all cases, and pointed out that the tumors were of slow growth, but could by expansion and erosion, give rise to middle ear or intracranial complications.

In 1936, Griefenstein[8] reported an asymtomatic VIIth nerve neuroma discovered at autopsy on a patient who had died following operation for pituitary tumor. There was no preceding history of facial paralysis or deafness.

In 1939 the first case in American literature was reported by Williams and Pastore.[9] This was a 59-year-old man with a left facial which developed over a period of one month four years previously. Five months before he appeared at the Mayo Clinic, he developed pre-auricular and mastoid pain with increasing deafness. His local otologist removed a "polyp" from the external auditory canal; but the symptoms were not relieved, and the polyp recurred. On examination he was found to have a complete left facial paralysis with

atrophy of the facial muscles. The left ear was deaf, and a polypoid mass filled the external auditory canal. There were no other abnormal findings. X-rays were reported as showing an area of irregular destruction in the bone in the left mastoid in an area overlying the lateral sinus. The polypoid mass in the external canal was biopsied and reported as "inflammatory ulcer and granulation tissue."

A radical mastoidectomy was done and a yellowish tumor mass extending into the facial canal was found and removed. The patient was given 12,000 mg. hours of radium. The facial paralysis persisted.

An additional case has been reported by Rejto,[10] but it is not available. In 1943, the literature was reviewed and an additional case reported by Roberts.[11] His was unusual in that the facial paralysis had been present for 30 years, deafness for 20, and purulent drainage for 15. He was operated upon for chronic mastoiditis, but a neurinomatous tumor which had eroded bone to become attached to the dura was found and removed. Recovery was good except for the persistent facial paralysis and deafness.

In 1944, Bogdasarian[12] reported a case in which facial paralysis had been present for five months, and vestibular function was normal. Hearing was reduced by air conduction but normal by bone conduction. A tumor mass bulging against the drum was biopsied and reported as neurinoma, so using a post-auricular approach the tumor was removed from the middle ear. The bone had been eroded by the tumor so that the dura was exposed but not invaded. Except for the persistent facial paralysis, the patient made a good recovery.

In 1946, Kettel[2] reported a VIIth nerve tumor discovered accidentally when the facial nerve was decompressed for "recurring Bell's palsy." He felt that certain aspects of the symptomatology in his case were different; *i.e.*, the paralysis improved and then recurred; no tumor could be seen in the ear, although paralysis had been present for years, and pain was a prominent symptom. In an interesting footnote, he states that the patient reported by Schroder[4] in 1931 was

still alive but unable to work because of "fits of fainting and fury." On four occasions he had been in mental hospitals, the fistula was closed, and the facial paralysis was still complete.

In 1953, Collins and Thomson[13] reported a case in which a tumor was excised which extended from .4 mms. proximal to the bifurcation of the nerve in the parotid to within 3 mms. of the genu. The bony roof of the canal was opened, the tumor removed, and a graft sutured to the divided ends of the nerve. The graft was successful, facial function reappearing in eight months, and the ultimate result was excellent as shown by photographs.

CONCLUSION.

The symptom-complex by which these tumors may be suspected while still confined to the middle ear of the mastoid has been described by Altmann. Obviously it is to be hoped that all cases will be diagnosed and the tumor removed while the lesion is still so confined, for in the stage prior to complete atrophy of the facial muscles, not only may the benign tumor be removed, but it is probable that the facial paralysis will be corrected by nerve graft. If, however, as in the two cases here reported, such a diagnosis is *not* made, one should be suspicious when the patient with a long standing facial paralysis begins to have either convulsive seizures or personality change. Since the lesion is very slow growing and because there is considerable available space in the middle fossa, pressure signs will occur late in the course of the disease. If such a lesion be suspected, the diagnosis may be confirmed by either angiography or ventriculography, but if the latter procedure is used, films to outline the temporal horns may be very valuable.

When the diagnosis of Bell's palsy is made it would be advisable for the patient to be seen by a competent otologist. Although neurilemmoma of the facial nerve in the middle ear is a rarity, its early diagnosis will save a complete facial paralysis and disfigurement. It seems feasible to remove the tumor and graft the nerve, if this is done before atrophy of the muscles is allowed to take place.

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TRENDS IN MOBILIZATION SURGERY.*†‡

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Trends in stapes mobilization surgery can be established only through the medium of a thorough statistical analysis of a large series of operated cases. I have little faith in statistics other than that they do establish a trend and, therefore, the title of this paper.

All of my stapes mobilization cases have been processed through the medium of I.B.M. equipment. Each 50 cases has been analyzed and charted on a graph. This graph allows us to visualize our results from month to month as we use various surgical techniques.

PROGRESS GRAPH.

The above graph depicts the percentage of stapes mobilization cases that have achieved a significant gain of 11 db or more in the three speech frequencies at the time of their three weeks' postoperative hearing test (see Fig. 1). Forty per cent of my first 50 cases achieved a significant gain at three weeks. At this time, the technique was predominately transcrural, using a mobilizing needle and a pneumatic hammer and working through the otoscope. For the first 300 cases, my results gradually improved until 60 per cent of the cases were achieving a significant gain at the time of their three weeks' postoperative test. At this point, I attempted to do the anterior crurotomy, as suggested by Fowler,[1] on 15 consecutive cases. Unfortunately, fractures of both the anterior and posterior crura resulted, thus accounting for the severe drop in our immediate results. The anterior crurotomy

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approach was discarded, and gradually our results again improved. At the 750 case level, a solid otosclerotic footplate was shattered with the pneumatic hammer applied directly in the center of the footplate. The patient became very vertiginous and two days later I realized that the patient had suffered an inner ear traumatic injury. At this point, the pneumatic hammer was discarded, and only the needle was used as a mobilizing instrument.

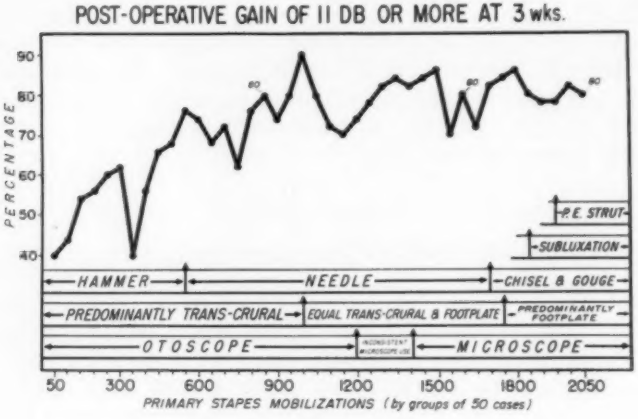

Fig. 1.

A study of the above graph reveals a stabilization in our results from the 800 case level to the 2,000 case level. Approximately 80 per cent of the cases were achieving a significant gain three weeks following surgery. This stabilization in results occurred in spite of the fact that we had changed our methods and techniques considerably from predominately the hammer and mobilizing needle to the needle alone, and later, to the chisels and gouges; from the otoscope to the microscope; from moderate mobility (Grade 2 motion without ligament tear or perilymph escape) to marked mobility (Grade 3 motion with ligament tear and perilymph escape); finally to subluxation routinely of all footplates (recently discarded).

From the 1,800 to 2,000 case level and beyond, we have been using the polyethylene strut placed directly on the shattered bluish footplate. In selected cases of solid footplate fixation, we have been using the drill and the vein graft technique, after the method of Shea.[2] (Vein graft series not sufficient to be statistically valid at this writing).

It would seem from the graph that successful three weeks' results in stapes mobilization surgery does not depend upon

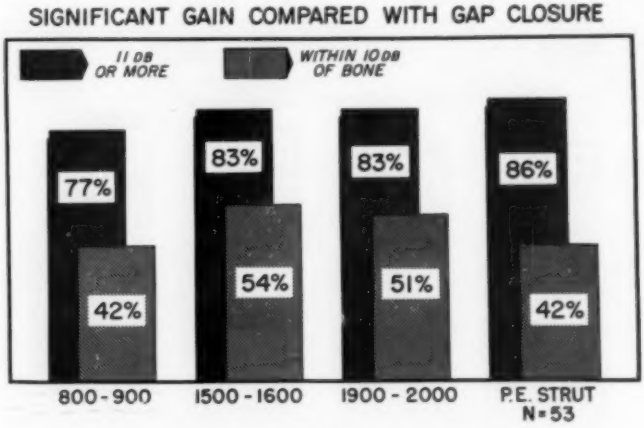

Fig. 2.

the instrumentarium used, or where or how the manipulating pressures are applied, as long as adequate mobilization of the footplate is achieved with an intact ossicular chain or adequate substitution of this ossicular chain. In this series the substitution used was the polyethylene strut with or without a vein graft. Other substitution techniques include the tantalum or steel wire (Schuknecht[3]) and the posterior crus repositioning (Juers[4]).

SIGNIFICANT GAIN COMPARED WITH TOTAL GAP CLOSURE.

A random spot study in groups of 100 cases of significant gain compared with total closure of the bone-air gap failed

to reveal any substantial difference in results (see Fig. 2), regardless of the various techniques used during this interval of time.

HEARING RESULT COMPARED WITH COCHLEAR FUNCTION.

For this random spot study, achievement of the 30 db level in the three speech frequencies was considered to be a satisfactory hearing improvement (see Fig. 3). Approximately

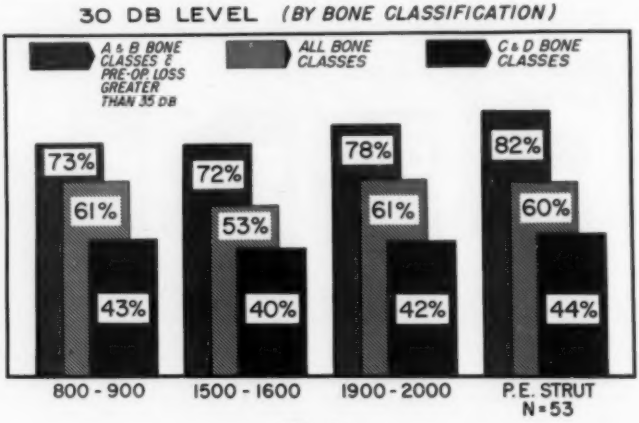

Fig. 3.

75 per cent of the cases with good cochlear function (A and B classification) closed their bone-air gap in the three speech frequencies to the 30 db level or better. Approximately 60 per cent of all of the mobilization cases achieved a 30 db level, and about 40 per cent of the cases with poor cochlear function (C and D classification) achieved this level. These percentages also remain fairly consistent from the 800 series to the 2,000 series, reconfirming the consistence in results in spite of the criteria of selection or the techniques used.

RESULTS BASED ON PERCENTAGE CLOSURE OF THE BONE-AIR GAP.

A study of the last 100 cases reported in this series reveals

approximately 85 per cent of the cases closed the bone-air gap, 25 per cent or more in the three speech frequencies; 70 per cent closed the bone-air gap 50 per cent or more, and 45 per cent closed the bone-air gap 75 per cent or more (see Fig. 4). Since using the polyethylene strut in more and more cases, these percentages are gradually improving.

The above series of statistical illustrations establish a trend; namely, that regardless of the technique used, if one achieves mobility of the footplate with ossicular continuity or with

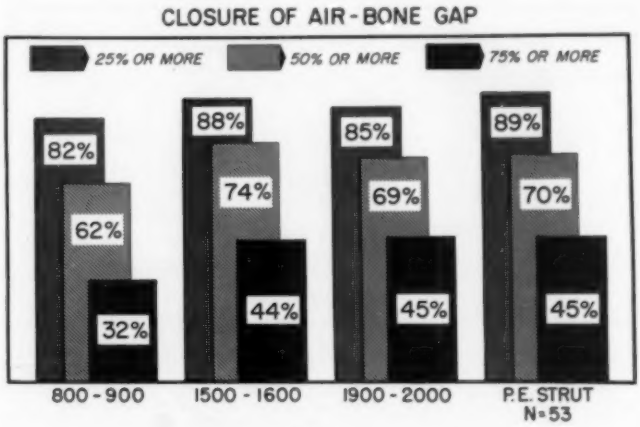

Fig. 4.

adequate substitution for this continuity, a fairly stable and constant type of hearing result will be achieved three weeks following surgery.

SIGNIFICANT GAIN AT THREE WEEKS COMPARED WITH OPERATING ROOM AUDIOMETRY.

A study of the above illustration tends to establish that the better the result in the operating room, the more likely one is to have a significant gain three weeks following surgery, in a routine mobilization procedure (see Fig. 5); however, approximately one-half of the cases that do not improve in

the operating room, still achieve a significant gain at three weeks. If there is a loss of 11 db or more in the three speech frequencies at the conclusion of surgery, only one out of five of this group shows a significant gain at the three weeks period.

At the conclusion of a routine mobilization procedure, we rely more on what we see and feel than on what the operating room audiometry reveals. If a polyethylene strut has been

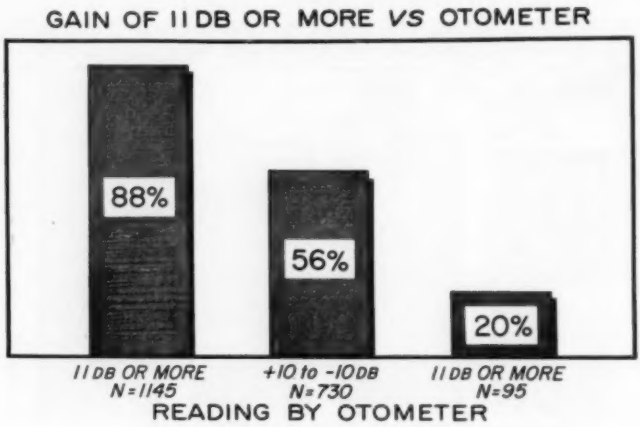

Fig. 5.

placed on a shattered bluish footplate, an immediate hearing improvement often does not occur. This is apparently due to the lack of mass movement and an inner ear seal. If a footplate is fenestrated or removed and a vein graft applied over the opening, an immediate significant gain, especially in the low tones is the usual response, apparently due to the presence of mass movement and an inner ear seal.

PERMANENCY STUDY.

The above illustration reveals that 90 per cent of the cases that closed the bone-air gap 50 per cent or more three weeks following surgery, maintained that level at four months; 84

per cent of this group maintained their hearing level at one year (see Fig. 6); therefore, of those cases that achieved their particular criteria three weeks after surgery, approximately 85 per cent are maintaining this criteria at one year.

A detailed study of our long-term results beyond one year, is being made at this time. Although I cannot give statistically valid figures at the time of this publication, it does seem apparent that the trend is toward gradual regression due to reankylosis.

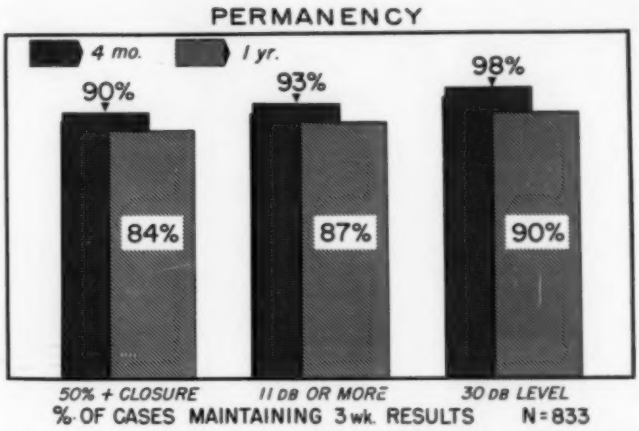

Fig. 6.

EARLY REANKYLOSIS.

Case Report. (Previously reported by Lindsay, et al.[5]). A 44-year-old woman with bilateral otosclerosis had a stapes mobilization performed in June, 1957 (see Fig. 7). Mobilization was accomplished transcrurally and resulted in normal Grade 2 footplate motion, without ligament tear or perilymph escape. This resulted in a 35 db improvement in hearing (and complete closure of the bone-air gap) four months after surgery. Eight months after surgery the patient died. Section (see Fig. 7) shows definite new bone formation in the annular ligament anteriorly.

In spite of the early evidence of reankylosis in this case, there was no clinical evidence of hearing decrease, and the audiogram failed to reveal any evidence of hearing regression.

It would seem logical to assume, however, that in due time, refixation would occur in this case.

Due to this gradual refixation trend, it seems logical that a higher percentage of permanent results following mobilization surgery can be achieved only through the use of a bypass, or substitution type, of surgical procedure, in order to avoid the active otosclerotic focus. At the present time, we apply gentle transcrural manipulating pressures only in those cases with

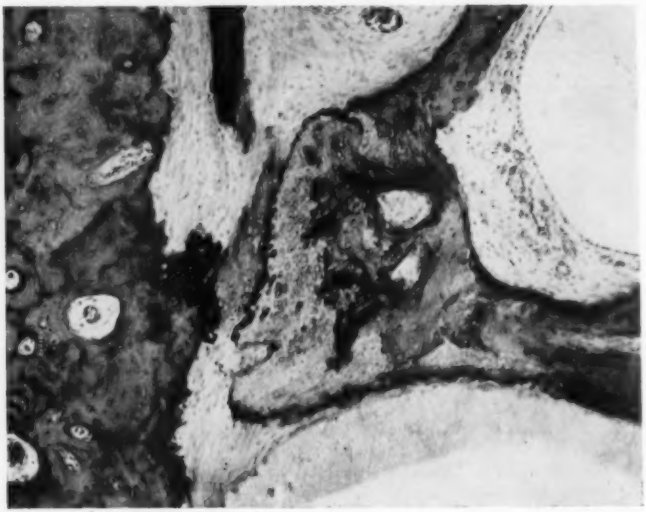

Fig. 7.

slight annular ligament involvement. The cases mobilize readily by this indirect method. In all other types of footplate fixation, we use a bypass or substitution technique, thereby avoiding the use of needles or chisels to fracture through the otosclerotic focus at the footplate margin. If refixation of a case with slight ligament involvement does occur, a revision is performed, using a bypass procedure.

BONE CONDUCTION SHIFT.

It is interesting to note that in the 76 per cent to 100 per

cent closure cases, a bone shift of 5.4 db in the three speech frequencies occurs. The better the result by air conduction, the greater the shift by bone conduction (see Table I).

SIGNIFICANT LOSSES (11 DECIBELS OR WORSE).

A study of the above illustration, indicates that as we gain more surgical experience, the percentage of cases that are made worse as a result of mobilization seems to be gradually

TABLE I.

BONE CONDUCTION SHIFT

26 - 50% Closure	+0.85	$p = 0.23$
51 - 75% Closure	+2.64	$p = <0.001$
76 - 100% Closure	+5.47	$p = \ll 0.001$
11 DB Gain	+3.51	$p = <0.001$

decreasing (see Table II). This decrease is primarily due to fewer fractured crura and the use of substitution procedures in the event both crura are inadvertently fractured.

The percentage of cases with inner ear involvement following stapes mobilization surgery seems to remain constant throughout our series. This is true in spite of the fact we have gone to the footplate much more as time went on. Approximately one-half of the cases that had further inner ear loss following mobilization surgery, were done by the transcrural approach without any direct manipulation of the footplate.

TABLE II.

SIGNIFICANT LOSSES
(MINUS 11 DB OR WORSE)

	AIR LOSS	NERVE	TOTAL
1955	3	1	4 (1:50)
1956	15	5	20 (1:40)
1957	3	6	9 (1:90)
1958	2	4	6 (1:150)
	23	16	39

TABLE III.

SEVERE LOSSES
(MINUS 20 DB OR WORSE)

NERVE LOSS	10
Total loss	*6*
Partial permanent	*3*
Returned to pre-op.	*1*
AIR LOSS	11
Known crural fracture	*9*
	21

SEVERE INNER EAR LOSSES—MINUS 20 DECIBELS OR MORE.

In this series of 2,000 mobilizations, there have been ten cases which developed a severe inner ear impairment. Of these ten cases, six had total loss of hearing. One of these six cases was the result of direct trauma in the operating room due to the use of the pneumatic hammer. Surgery was routine and uneventful in the other nine cases. An analysis

TABLE IV.

	PRE-OP.				SURGERY							POST-OP.				COMMENT
YEAR	AGE	BONE	AIR	VERTIGO	TECHNIQUE	OTOMETER	MOBILIZATION			VERTIGO	CRURAL FRACTURE	VERTIGO	INFECTION	HEARING	TIME	
							TC	FP	DEGREE							
'56	35	C	43	0	0	-22	/		3	//		/	0	70	3 wk.	Gradual improvement to pre-op level in 2 mos. vasodilator R_x.
'56	63	A	40	0	0	-3	/		3	/		//	0	--	1 wk.	Continued vertigo despite vasodilator therapy.
'56	61	A	40	?	0	-15	/		4	///	/	///	/	77	3 wk.	Continued vertigo despite vasodilator therapy.
'57	23	A	47	0	M	-14		/	3	0		///	0	--	1 wk.	Revision mobilization on a congenital footplate fixation.
'57	40	A	50	0	M	/15	/		2	/	/	/	0	--	6 wk.	
'57	37	A	35	/	M	-15		/	3	/		0	0	--	3 mo.	
'58	61	D	77	///	M	0	/		2	0		/	0	--	1 day	
'58	59	A	65	?	M	/23		/	4	/	/ strut	//	/	65	3 wk.	Bone dropped 20 db. Air remained at 65 db.
'58	62	B	45	/	M	0		/	3	0		///	0	--	3 wk.	Vertigo for 6 mos. despite vasodilator therapy.
'58	49	C	45	?	M	-2		/	4	0	/	0	0	68	11 wk.	

TECHNIQUE { M = Microscope, O = Otoscope } MOBILIZATION { TC = Transcrural, FP = Footplate } DEGREE { 2 = No ligament tear, 3 = Partyeigh escape and subluxation (ligament tear), 4 = Shattered footplate }

of the other nine cases revealed that two were the result of infection, and the remaining seven were apparently vascular in type and developed from one week to as long as six weeks following surgery (see Table III). In each instance, the patient was hearing and suddenly developed severe tinnitus with or without vertigo, followed by loss of inner ear function. Of these seven cases that had an apparent vascular accident, only three had direct footplate manipulation.

DETAILED ANALYSIS OF CASES WITH SEVERE INNER EAR LOSS.

When one considers the number of cases reported in this series, the incidence of severe inner ear loss is not great (see Table IV). Because of this complication, however, one should not, except in most unusual circumstances, operate upon the better ear or operate upon both ears simultaneously.

Fig. 8.

FOOTPLATE PATHOLOGY IN RELATION TO SURGICAL TECHNIQUE.

We classify our footplate pathology into four main categories: Ligament, anterior, bipolar and solid otosclerotic footplate fixation. It has been our experience that we cannot accurately and consistently forecast the type of footplate fixation we may encounter by means of the preoperative audiogram.

At the time of surgery, one must carefully analyze the type of footplate pathology that is present before proceeding with the act of mobilization.

LIGAMENT TYPE OF FIXATION.

It is difficult to visualize any evidence of otosclerotic in-

volvement in this type of case (see Fig. 8). What otosclerotic involvement is present is very minute and is located in the annular ligament itself. Mobilization usually occurs readily by the indirect method. Since the otosclerotic process is quite minute, the incidence of refixation in this type of case seems to be very low.

Rosen[6] recently reported on the permanency of his first 100 successfully mobilized cases. All were mobilized by the indirect (original) Rosen technique. He stated that less than

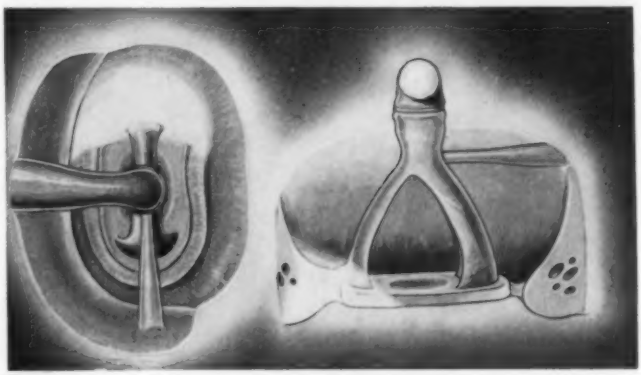

Fig. 9.

15 per cent revealed regression five years after surgery. I believe these cases were largely of the ligament type and, therefore, the low regression rate reported by the author.

ANTERIOR FOOTPLATE FIXATION.

If the footplate reveals an anterior type of otosclerotic fixation, transcrural pressure directed through the posterior crus will allow a slight amount of posterior mobility due to flexibility of the fixed anterior crus (see Fig. 9). In this type of case, one may attempt transcrural mobilization. If successful, either a fracture through the anterior otosclerotic process or a spontaneous anterior crurotomy will result. If transcrural mobilization cannot be achieved, one may apply a

needle, chisel or gouge directly on the otosclerotic process at the anterior footplate margin. It is known that many patients whose stapes were mobilized through the active otosclerotic process in years gone by continue to maintain their original hearing. At present we do either the anterior crurotomy (Fowler technique[1]), or preferably, a bypass type of procedure in cases with anterior fixation. The bypass procedure may be in the form of a posterior crural reapposition as advocated by Juers,[4] a tantalum wire prosthesis as advocated

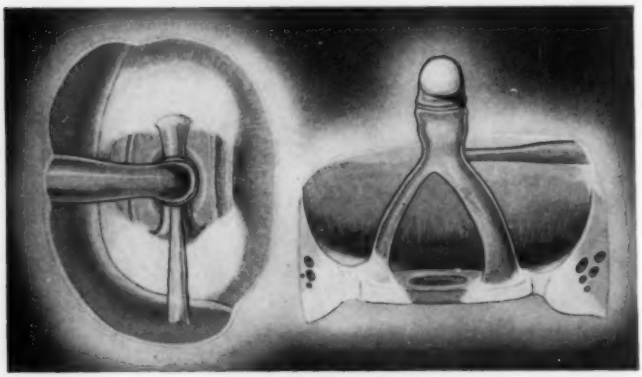

Fig. 10.

by Schuknecht,[3] a polyethylene strut and vein graft procedure, as advocated by Shea,[2] or a polyethylene strut placed directly on the bluish footplate, followed by shattering of the plate as preferred by the author. At the present time we are doing oval window fenestrations with the vein graft, or gelfoam in all but ligament fixation cases. This series is being done to compare the results with those obtained by placing the strut on the shattered bluish footplate. The results of this series will be reported at a later date.

BIPOLAR FIXATION.

Bipolar fixation occurs more often than any other type in the author's experience. In this instance, gentle manipula-

tion applied by the transcrural approach reveals total and complete immobility. One does not notice any flexibility of either crus. Mobilization in bipolar cases can be achieved only by fracturing directly through the active focus, and this results in either an anterior or posterior crurotomy. Often both crura are inadvertently fractured.

In our experience (see Fig. 10), bipolar fixation cases tend to refix readily and are most unsatisfactory if one applies the usual manner of indirect or direct techniques of mobiliza-

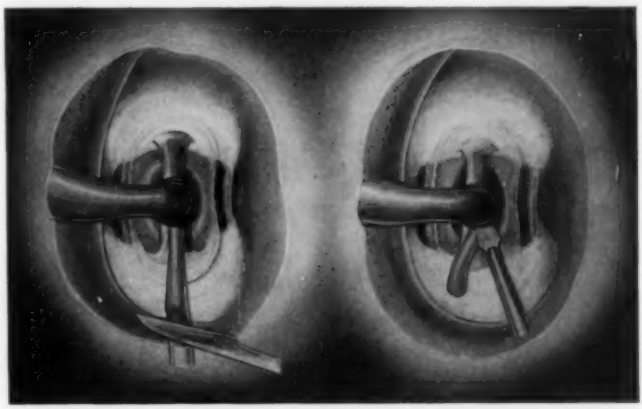

Fig. 11.

tion; consequently, we routinely remove the stapes crura and institute a polyethylene strut bypass procedure.

Severance of the stapedius tendon and separation of the inco-stapedial joint (see Fig. 11).

Removing the stapes arch and crura (see Fig. 12).

Measuring distance between the bluish central portion of the footplate and the incus (see Fig. 13).

Insertion of the Polyethylene Strut.

A previously prepared No. 90 polyethylene strut of the correct length is carefully placed into position (see Fig. 14).

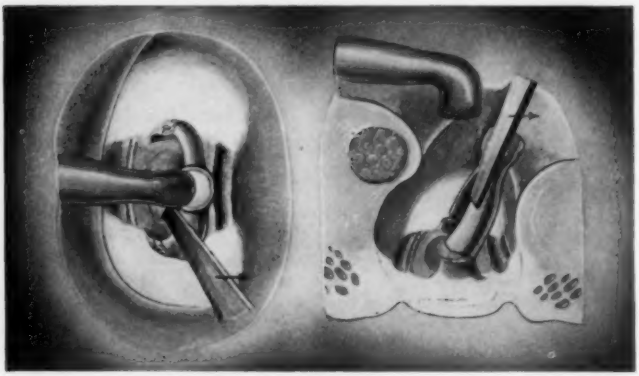

Fig. 12.

Fig. 13.

The length of the strut must be exact and a small hook is used carefully to lift the incus to allow the strut to take its position directly under the lenticular process. The strut must be under slight tension between the incus and bluish portion of the footplate.

SHATTERING OF THE FOOTPLATE.

After the polyethylene strut has been placed in position

Fig. 14.

Fig. 15.

with adequate tension between the incus and the footplate, a small chisel is carefully used to shatter the bluish portion of the footplate in several locations (see Fig. 15). Small pledgets of gelfoam may be placed about the footplate area, and the ear drum is replaced.

We have had occasion to revise a number of previously mobilized cases. In most instances, the bluish portion of the footplate which was previously shattered remains shattered and movable. Apparently, this portion of the footplate does not have the osteogenic regrowth tendency encountered in the otosclerotic focus.

SOLID OTOSCLEROTIC FOOTPLATE FIXATION.

Until recently when we encountered this type of fixation, we would attempt mobilization with a chisel and gouge. If

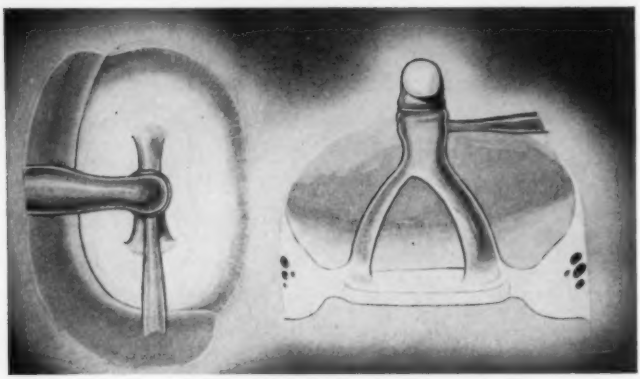

Fig. 16.

successful, rapid refixation frequently occurred. In many instances, however, mobilization could not be attained, and the fenestration operation was carried out subsequently (see Fig. 16); or if the patient was not suitable for fenestration, the continued use of a hearing aid was advocated.

FENESTRATION OF SOLID FOOTPLATE.

At the present time, we routinely use a diamond drill to fenestrate, or drill out the solid footplate as advocated by my brother.[7] A vein graft (Shea[2]) or other substance, such as gelfoam is used to cover the oval window, and a polyethylene strut is placed into position. Since using this method, we

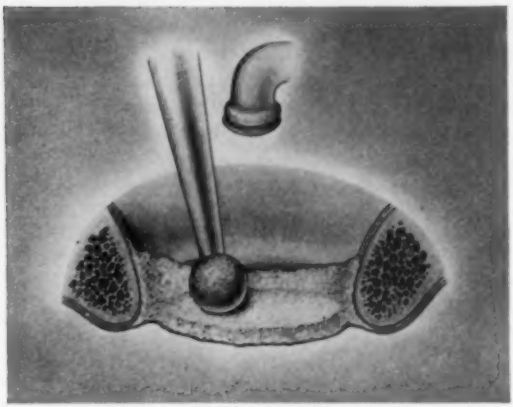

Fig. 17-a.

Fig.17-b.

have found it to be a very satisfactory solution to this type of case (see Fig. 17-a and 17-b). Needless to say, this technique is technically difficult and not without risk to the inner ear.

We owe a debt of gratitude to John Shea for his pioneering

in this field of substitution surgery for the stapes and stapes footplate. He first presented the thought of substitution surgery some three years ago in a discussion at the meeting of the American Laryngological, Rhinological and Otological Society in Montreal.[8]

FRACTURED CRURA VS. POLYETHYLENE STRUT.

The use of the polyethylene strut has allowed us not only to bypass the otosclerotic process, but if both crura are inadvertently fractured during a routine mobilization procedure,

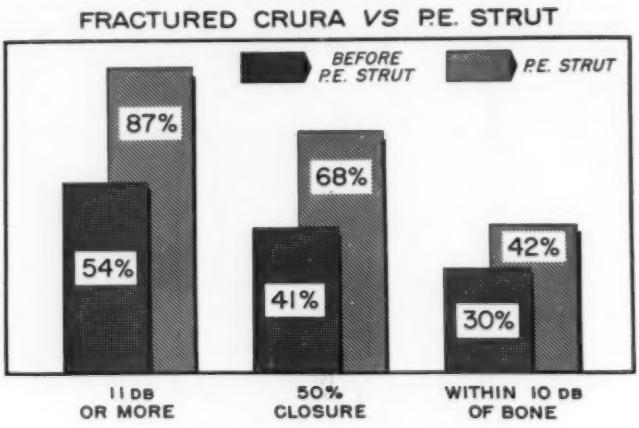

Fig. 18.

the polyethylene strut can be used as a crural substitute (see Fig. 18). The accompanying illustration reveals that if both crura are fractured, the patient's chances of success are lessened by one-third. The use of the polyethylene strut has altered this picture so that the result is now essentially the same in cases with fractured crura as it would have been had the fractures not occurred.

REVISIONS BEFORE AND AFTER THE POLYETHYLENE STRUT.

A study of our revisions before and after the use of the

polyethylene strut is, indeed, most illuminating (see Fig. 19). The polyethylene strut has resulted in our revisions being as successful as our original stapes mobilization cases. If the failure of the original stapes mobilization cases was due to fractured crura, the polyethylene strut acts as a substitute. If the cause of failure of the original procedure was due to refixation, the polyethylene strut allows a bypassing type of operation at the time of revision.

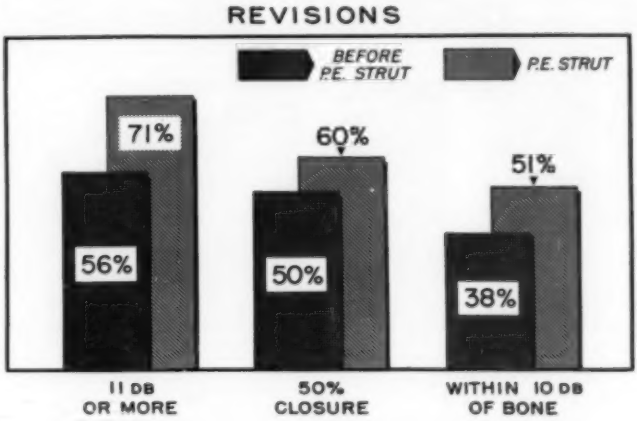

Fig. 19.

FOOTPLATE MOBILITY VS. ULTIMATE HEARING RESULT.

It seems apparent that whether one has a Grade 2 mobility (without tear of annular ligament or perilymph escape) at the conclusion of the operation, or one has a Grade 3 mobility (ligament tear and perilymph escape), there is little difference as far as the ultimate performance is concerned (see Fig. 20). If any conclusions can be drawn, Grade 2 mobility has a slightly better chance of obtaining a significant gain, but no better chance of maintaining this gain than does the Grade 3 case; likewise, subluxation of the footplate does not seem improve the ultimate hearing result.

The tendency of most surgeons doing this work is to mobilize

the stapes footplate to the point of marked mobility (like a bobbing cork). This marked degree of motion is not physiological and is far in excess of the movement of a normal stapes. In the routine stapes mobilization procedure as carried out in a case of ligament fixation, the author no longer intentionally proceeds beyond a Grade 2 type of motion.

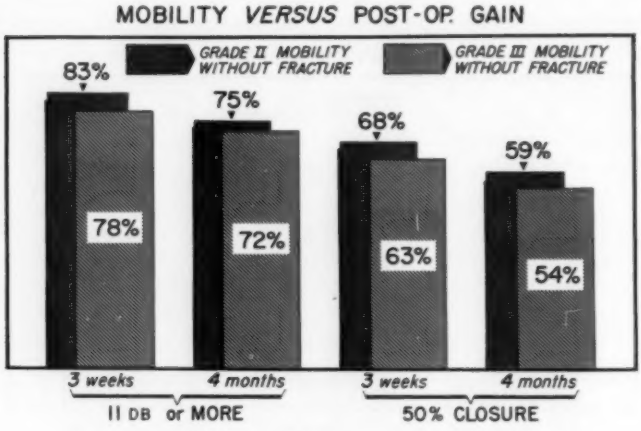

Fig. 20.

SUMMARY.

What then are the trends in mobilization surgery?

The trend of the past has been represented predominately by indirect mobilizing pressures exerted through the crura.

The trend of the present is represented by both direct and indirect mobilizing pressure on the footplate region.

The trend of the future will be to continue those methods that have given successful results in the past (indirect mobilization in ligament fixation cases). In anterior and bipolar fixation, the future trend will be to avoid the active otosclerotic focus by using a by-pass procedure. In extensive otosclerosis, removal of the footplate, together with the oto-

sclerotic focus (oval window fenestration) will become more commonplace.

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CHOLESTEATOMA OF THE EXTERNAL AUDITORY CANAL.*†

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On May 11, 1951, Mrs. J.C.D., aged 70, complained to me of deafness and discharge in both ears. Her story of ear trouble dated back 22 years, during which time she had received a diagnosis of "fungus" (supposedly of the ears), had become somewhat hard of hearing in the right ear, and had had the right ear washed out on one occasion, following which she had developed the only earache of her lifetime. Other history was rather unimportant except that she had headaches and a productive cough.

On examination, the right ear was found not to be discharging, although some amber fluid could be seen in the right middle ear through the intact tympanic membrane. The left external auditory canal contained a considerable amount of heavy discharge, there was external otitis especially involving the inferior and posterior canal walls, and there was an anterior marginal perforation through which mucus was pulsating. The hearing tests indicated conduction and nerve deafness similar in the two ears.

Twelve days and two treatments later, there was no discharge from the left ear, no fluid could be seen in the right middle ear, and the hearing was clinically improved. She was appreciative, remunerative, and procrastinative, returning for treatment seven months later, at which time again there was external otitis of the left ear with a large amount of material coming from the region of the anterior marginal perforation.

X-ray films were a bit surprising in demonstrating moderate

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sized cellular mastoids, which did not look too different from each other. The left mastoid did have thicker septal bone, but there was no destruction, and no indication of cholesteatoma formation, which did not explain why some of the material that was wiped from the canal appeared to be cholesteatoma pus. Again she recovered, and returned at two to six month intervals with the same findings and the same favorable response to treatment.

On the occasion of a visit 15 months later, it was noted that she had the same type of discharge in the left canal, but there was no discharge coming through the open anterior perforation in the left tympanic membrane. This canal discharge had its usual viscosity and foul odor, and there was the same point of excoriated external canal skin. Beneath the exudate on the posterior canal wall the bone was denuded and rough. The exudate seemed typical of cholesteatoma. There was no posterior or superior perforation of the tympanic membrane, and no discharge from the middle ear.

Without enthusiasm, I cross-filed this as a cholesteatoma of the external auditory canal, thinking little of it as an entity, having seen her when there was mucoid discharge from the middle ear, and also considering her age of 70 and the possible trophic changes; nevertheless, I could not explain why there was no evidence of cholesteatoma in the middle ear, why the X-ray films showed no evidence of cholesteatoma of the mastoid antrum and why the impaired hearing was so alike in the two ears. Since it would be much easier to think about this explanation tomorrow, and get on with the next patient today, this was painstakingly done and the situation adequately forgotten.

Seven months later, Mr. H. W. appeared with intact tympanic membranes, normal hearing, and a peculiar type of cerumen which adhered so closely to the right posterior inferior canal wall, that it took two treatments to remove it, following which rough exposed bone of the canal was visible. I was fascinated to see that the medial end of the canal had undercut the tympanic membrane so much that the inferior part of the annulus tympanicus was relatively high in the canal. The underside of the cerumenous plug and the thin

covering of the rough bone resembled the matrix that covers the bone of the mastoid antrum, in cases of cholesteatoma.

One-and-one-half years after this, Mr. J.T.F. came in with much the same situation as Mr. H.W., except that his canal was more deeply eroded with exposure of mastoid cells. I decided that it was time to quit waiting until tomorrow to think.

Since 1951, nine such patients have been observed by me, each with his individual characteristics, but all having one thing in common—an area in the external auditory canal

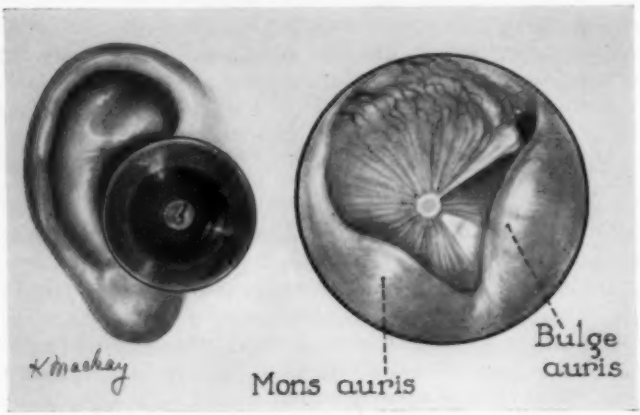

Fig. 1. The right external auditory canal as it often appears. The complete membrane is rarely seen.

where the bone is covered by a thin, white, sickly-looking membrane, from which seems to come a cholesteatoma type of discharge, complete with heavy flakes and foul odor.

There were four males and five females. The ages ranged from 19 to 77. The left ear was affected seven times, the right twice. The most consistent accompanying condition was the noticeable vasomotor rhinitis with or without the productive bronchiectatic cough, which was found in six of the nine patients. This would be a point in favor of the theory proposed by Van Canaghem, Harpman, and others. I have not seen where this condition could be directly con-

nected with cholesteatoma of the external canal. All patients were white.

LITERATURE.

Prior to the Twentieth Century, most of the literature on this subject was written in German. Hessler's article must have been the classic. In 1953, J. J. Biber presented his splendid article in which he gave a very complete summary of the works of his predecessors, whose collective opinions were that there is diversity of thought as to what causes cholesteatoma, where cholesteatoma starts, whether it has the right name, and whether there is any such thing as primary cholesteatoma of the external canal in the first place.

So far as I know, the most recent article was written by Col. Byron G. McKibben, U.S.A., and published in the May, 1958, issue of the *Archives of Otolaryngology*. In it he described one case which occurred in a Negro. Just last month, I received a cordial letter from the Colonel in which he stated that he feels now that he might prefer a split thickness skin graft in the stenosing external canal rather than the modified radical mastoidectomy.

DESCRIPTION.

There are certain definite physical characteristics to be found in the cholesteatomatous, human auditory canal. To the otolaryngologist, this is such a common channel of investigation, that the details of its shape are rarely even considered. The circuitous route to the tympanic membrane, probably so shaped for protection, begins with the springing forward of the conchal cartilage, which is overlapped by the backward inclination of the tragal cartilage. This barrier is quickly eliminated by inserting the aural speculum. If one then should look directly through the speculum on a horizontal line, without moving the line of vision or the speculum, he would note that the tympanic membrane is usually invisible in its anterior one-fourth, the reason being the backward bulging of the bone of the anterior canal wall, just behind the temporomandibular joint, which we might designate as the *bulge auris*. The lower one-eighth to one-fourth of the tympanic membrane

is hidden by a more or less mounding up which we might call the *mons auris*. Medial to the mons, the bony canal declines to form a sulcus on the lateral side of the annulus tympanicus, inferiorly; therefore, the most consistently visible part of the tympanic membrane from a direct horizontal view is the posterior superior segment.

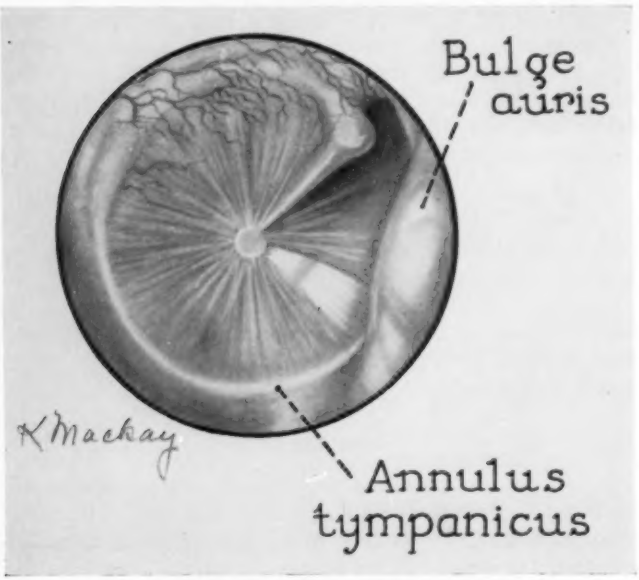

Fig. 2. The size and shape of the normal external auditory canal varies. The mons may not be present, but the bulge is almost always seen.

The most common variation is the height of the mons, which in some cases (far less than 50 per cent in my experience), may be hardly elevated at all. Then the canal is large, and the tympanic membrane can be seen in its entirety except for a bit of the anterior part of the annulus. Such an auditory canal may be thought of as the *mobilizer's delight*, for obvious reasons. Seldom does the normal canal undercut the annulus tympanicus more than perhaps two millimeters; but, where there is cholesteatoma of the external canal, the annulus may

be undercut a full ten millimeters, even to the extent of exposing mastoid cells, in which instance the inferior aspect of the annulus appears to be raised to the middle of the medial end of the external auditory canal.

The surface of the bone of the lesion is irregular. When the thin, unhealthy appearing epithelium which covers this is removed, the underlying bone often presents a shiny appearance, and there may be a small amount of bleeding. An exposed mastoid cell is always covered by what appears to be its individual mucous membrane lining. I have never seen fluid or cholesteatoma in one of these cells, and I have never entered one of these cells in search of either.

Although some of the previous writers have considered the anterior canal wall as the favorite site for the focal point of this lesion, in my cases, the floor and contiguous posterior wall have most often suffered.

Other findings of this condition are:

1. A heavy cerumenopurulent, foul aural discharge which is not attended by as much tenderness and pain as is found in ordinary external otitis (pain and tenderness are not common).

2. An intact tympanic membrane, or at least one in which there is no obvious connection with the external canal lesion.

3. The hearing in the affected ear is more in keeping with the hearing of the unaffected ear, whether or not this be normal, than with a hearing curve that indicates involvement of its conduction mechanism.

4. X-ray findings not indicating cholesteatoma of the middle ear or mastoid.

Tissue for microscopic examination has been recovered from five of these nine patients. Local anesthesia by injection is used. Often, the canal lesion is covered by a cerumenopurulent epithelial plug which is fitted into the bony excavation. When this is removed, the edges of the lesion may be clean; but, as a rule, there is a border of granulations.

The biopsy is obtained by elevating the granulomatous edge,

including, if possible, some of the epithelium that covers the lesion. The microscopic findings have been quite uniform. Sections from the margins show heavy, limited epithelium reported as hyperkeratinization. Those from the epithelium overlying the rough bone show connective tissue dermis with a covering of thin epidermis, on which is amorphous desquamation, which is affectionately known to us as *gunk*. Histologically, this cannot be differentiated from the gunk that is seen overlying the epithelium of an inclusion cyst, except that the latter is more tightly packed. Indeed, the epithelium of the canal lesion does not differ primarily from the normal skin of the bony canal wall. In only one case did the pathologist question activity enough for him to advise rebiopsy at an appropriate time.

COMMENT.

Granting that there is at present no known cause for cholesteatoma of the temporal bone, it may be that cholesteatoma of the external auditory canal is an entity which results either from local periosteitis with subsequent superficial devitalization of the underlying bone, or the reverse in which, for some reason unexplained to me, the tympanic bone becomes unhealthy. It may be that the temporal bone is subject to irreversible damage in infections, because of its cellular makeup. It may be that the invagination of the epithelium to form the external auditory canal makes this a type of potential inclusion cyst which does not withstand the stress of long standing infection. I favor the speculative periosteitis, but I am not convinced that it necessarily develops from the discharge that flows over it from otitis media and mastoiditis through a perforated tympanic membrane.

This subject initiates a rather important question. According to current gossip, the cholesteatomatous cavity of the mastoid bone becomes larger because of the pressure brought to bear on the bone by the cholesteatoma. In the external canal, there is bone erosion, but there is no obvious pressure. Could the gossip be wrong?

Contrary to a prevailing opinion, I do not think that this condition is extremely rare. More likely it is that the average

patient with this disease is considered to have simple detritus for which the usual treatments are administered.

TREATMENT.

Generally speaking, conservative treatment is preferred. The patient can be made asymptomatic by cleanliness. He can help by using a simple cleansing irrigation such as the boric acid-alcohol solution; but, an occasional professional debridement is necessary. No operative procedure has been carried out in any of these patients. Should an operation be advised, an extensive modified radical mastoidectomy with removal of all mastoid cells would be necessary. I cannot conceive of any advantage. Even though there does not seem to be a tendency for the eroded bone to heal, progression of the disease is significantly slow and splendidly inconsequential.

SUMMARY.

1. There are reasons to believe that *cholesteatoma of the external auditory canal* is an entity.

2. A general report covering the pertinent findings observed in a series of nine patients has been presented.

3. The most important finding is erosion of the bony floor of the external auditory canal.

4. Treatment has been conservative.

5. The cause is unknown.

"Finally, brethren, whatsoever things are true, honest, just, pure, lovely, of good report; if there be any virtue, and if there be any praise, think on these things." (Philippians 4:8). So said the Apostle Paul.

I express my appreciation to pathologists H. Vincent Bell, M.D., and Lester Forbes, M.D., Georgia Baptist Hospital, Atlanta, Ga., and to the medical illustrator, Miss Kathleen MacKay, and photographer, Joe T. Jackson, Emory University, Atlanta, Ga., for their valuable aid in preparing this article.

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Secretary:
Meeting:

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY.

President: Dr. Van D. Rathgeber.
Vice-President: Dr. William Skokan.
Secretary-Treasurer: Dr. Paul Rockwell.

GREATER MIAMI EYE, EAR, NOSE AND THROAT SOCIETY.

President: Dr. Mariano C. Caballero.
Vice-President: Dr. Joseph Freeman.
Secretary-Treasurer: Dr. H. Carlton Howard.
Meeting: Quarterly in March, May, October and December on the second Thursday of the month, 6:30 P.M., at the McAllister Hotel, Miami, Fla.

INTERNATIONAL BRONCHOESOPHAGOLOGICAL SOCIETY.

President: Dr. Jo Ono, Tokyo, Japan.
Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa., U. S. A.
Meeting:

KANSAS CITY SOCIETY OF OTOLARYNGOLOGY AND OPHTHALMOLOGY.

President: Dr. Clarence H. Steele.
President-Elect: Dr. Dick H. Underwood.
Secretary: Dr. James T. Robison, 4620 J. C. Nichols Parkway, Kansas City, Mo.
Meeting: Third Thursday of November, January, February and April.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Max E. Pohlman.
Secretary-Treasurer: Dr. Wendell C. Irvine.
Chairman of Ophthalmology Section: Dr. Carroll A. McCoy.
Secretary of Ophthalmology Section: Dr. Philip D. Shanedling.
Chairman of Otolaryngology Section: Dr. Robert W. Godwin.
Secretary of Otolaryngology Section: Dr. Francis O'N. Morris.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd., Los Angeles, Calif.
Time: 6:30 P.M. last Monday of each month from September to June, inclusive—Otolaryngology Section. 6:30, first Thursday of each month from September to June, inclusive—Ophthalmology Section.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY.

President: Dr. Fred D. Hollowell, Lamar Life Bldg., Jackson, Miss.
Secretary: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.
Meeting:

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

Chairman: Members serve as chairmen in alphabetical order monthly.
Secretary-Treasurer: Dr. Roland H. Myers, 1720 Exchange Bldg., Memphis, Tenn.
Assistant Secretary-Treasurer: Dr. William F. Murrah, Jr., Exchange Bldg., Memphis, Tenn.
Meeting: Second Tuesday in each month at 8:00 P.M. at Memphis Eye, Nose and Throat Hospital.

MEXICAN ASSOCIATION OF PLASTIC SURGEONS.

President: Dr. Cesar LaBoide, Mexico, D. F.
Vice-President: Dr. M. Gonzales Ulloa, Mexico, D. F.
Secretary: Dr. Juan De Dios Peza, Mexico, D. F.

MEXICAN SOCIETY OF OTOLARYNGOLOGY.

President: Dr. Rafael Giorgana.
Secretary: Dr. Carlos Valenzuela, Monterey 47, Mexico 7, D. F.

MISSISSIPPI VALLEY MEDICAL SOCIETY.

President: Dr. Arthur S. Bristow, Princeton, Mo.
Secretary-Treasurer: Dr. Harold Swanberg, Quincy, Ill.
Assistant Secretary-Treasurer: Dr. Jacob E. Reisch, Springfield, Ill.

NETHERLANDS SOCIETY OF OTO-RHINO-LARYNGOLOGY.
(Nederlandsche Keel-Neus-Oorheelkundige Vereeniging.)

President: Dr. H. Navis, Sonsbeekweg 6, Arnhem.
Secretary: Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam.
Treasurer: Mrs. F. Velleman-Pinto, Jac. Ohrechtstr. 66, Amsterdam.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY.

President: Dr. J. C. Peele, Kinston Clinic, Kinston, N. C.
Vice-President: Dr. George E. Bradord, Winston-Salem, N. C.
Secretary-Treasurer: Dr. J. D. Stratton, 1012 Kings Drive, Charlotte 7, N. C.
Meeting:

NORTH OF ENGLAND OTOLARYNGOLOGICAL SOCIETY.

President: Mr. G. L. Thompson, 16 Ramshill Road, Scarborough, Yorkshire.
Vice-President: Mr. J. H. Otty, Frizley Old Hall, Frizinghall Road, Bradford, Yorkshire.
Secretary and Treasurer: Mr. R. Thomas, 27 High Petergate, York, Yorkshire.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. David D. DeWeese, 1216 S. W. Yamhill St., Portland 5, Ore.
Secretary-Treasurer: Dr. Paul B. Myers, 223 Medical Dental Bldg., Portland 5, Ore.
Meeting: Fourth Tuesday of each month from September through May, Henry Thiele Restaurant, 23rd and W. Burnside, Portland, Ore.

OTOSCLEROSIS STUDY GROUP.

President: Dr. E. P. Fowler, Jr., 180 Fort Washington Ave., New York 32, New York.
Secretary-Treasurer: Dr. Arthur L. Juers, 1018 Brown Building, Louisville 2, Ky.
Meeting: Palmer House, Chicago, Ill., October 11, 1959.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY.

President: Dr. John F. Tolan, 1118 - 9th Ave., Seattle 5, Wash.
Secretary-Treasurer: Dr. Homer E. Smith, 686 Twelfth Ave., Salt Lake City, Utah.
Meeting:

PAN AMERICAN ASSOCIATION OF OTO-RHINO-LARYNGOLOGY AND BRONCHO-ESOPHAGOLOGY.

President: Dr. Paul Holinger, 700 No. Michigan Blvd., Chicago, Ill.
Executive Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa., U. S. A.
Meeting: Seventh Pan American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology.
Time and Place: Miami, Fla., March, 1960.

PHILADELPHIA LARYNGOLOGICAL SOCIETY.

President Dr. John J. O'Keefe.
Vice-President: Dr. Joseph P. Atkins.
Secretary: Dr. William A. Leil.
Executive Committee: Dr. Harry P. Schenck, Dr. Benjamin H. Shuster, Dr. William A. Leil, Dr. William J. Hitschler, and Dr. Chevalier L. Jackson.

PHILIPPINE SOCIETY OF OTOLARYNGOLOGY AND BRONCHO-ESOPHAGOLOGY.

President: Dr. Macario G. Tan, 426 Evangelista, Manila, P. I.
Vice-President: Dr. Ariston G. Bautista, 460 Isaac Peral, Manila, P. I.
Secretary-Treasurer: Dr. Angel Enriquez, American Hospital, Aduana St., Manila, P. I.

PITTSBURGH OTOLOGICAL SOCIETY.

President: Dr. Emory A. Rittenhouse, 203 Masonic Bldg., McKeesport, Pa.
Vice-President: Dr. Carson S. Demling, 513 Jenkins Bldg., Pittsburgh 22, Pa.
Secretary-Treasurer: Dr. Clyde B. Lamp, 8101 Jenkins Arcade, Pittsburgh 22, Pa.

PORTUGUESE OTORHINOLARYNGOLOGICAL SOCIETY.

President: Dr. Albert Luis de Mendonca.
Secretary: Dr. Antonio da Costa Quinta, Avenida, de Liberdale 65, 1° Lisbon.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Clifton E. Benson, Bremerton, Wash.
President-Elect: Dr. Carl D. F. Jensen, Seattle, Wash.
Secretary: Dr. Willard F. Goff, 1215 Fourth Ave., Seattle, Wash.

SIXTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST.

Meeting: University of Vienna, August 29 to September 1, 1960.

RESEARCH STUDY CLUB OF LOS ANGELES, INC.

Chairman: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Treasurer: Dr. Norman Jesberg, 500 So. Lucas Ave., Los Angeles 17, Calif.
Otolaryngology: Dr. Russell M. Decker, 65 N. Madison Ave., Pasadena 1, Calif.
Ophthalmology: Dr. Warren A. Wilson, 1930 Wilshire Blvd., Los Angeles 57, Calif.
Mid-Winter Clinical Convention annually, the last two weeks in January at Los Angeles, Calif.

SECTION OF OTOLARYNGOLOGY OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA.

Chairman: Dr. J. L. Levine.
Vice-Chairman: Dr. Russell Page.
Secretary: Dr. James J. McFarland.
Treasurer: Dr. Edward M. O'Brien.
Meetings are held the second Tuesday of September, November, January, March and May, at 6:30 P.M.
Place: Army and Navy Club, Washington, D. C.

SCOTTISH OTOLARYNGOLOGICAL SOCIETY.

President: Dr. F. T. Land, 13 Newton Place, Glasgow, C. 3.
Secretary-Treasurer: Dr. J. F. Birrell, 14 Moray Place, Edinburgh.
Assistant Secretary: Dr. H. D. Brown Kelly, 11 Sandyford Place, Glasgow, C. 3.

SOCIEDAD COLUMBIANA DE OFTALMOLOGIA Y OTORRINOLARINGOLOGIA (BOGOTA, COLUMBIA).

Presidente: Dr. Alfonso Tribin P.
Secretario: Dr. Felix E. Lozano.
Tesorero: Dr. Mario Arenas A.

SOCIEDAD CUBANA DE OTO-LARINGOLOGIA.

President: Dr. Reinaldo de Villiers.
Vice-President: Dr. Jorge de Cárdenas.
Secretary: Dr. Pablo Hernandez.

SOCIEDAD DE ESTUDIOS CLINICOS DE LA HABANA.

Presidente: Dr. Frank Canosa Lorenzo.
Vice-Presidente: Dr. Julio Sanguily.
Secretario: Dr. Juan Portuondo de Castro.
Tesorero: Dr. Luis Ortega Verdes.

SOCIEDAD DE OTORRINOLARINGOLOGIA Y BRONCOESOFAGOSCOPIA DE CORDOBA.

Presidente: Dr. Aldo Remorino.
Vice-Presidente: Dr. Luis E. Olsen.
Secretario: Dr. Eugenio Romero Diaz.
Tesorero: Dr. Juan Manuel Pradales.
Vocales: Dr. Osvaldo Suárez, Dr. Nondier Asis R., Dr. Jorge Bergallo Yofre.

SOCIEDAD DE OTO-RINO-LARINGOLOGIA, COLEGIO MEDIO DE EL SALVADOR, SAN SALVADOR, C. A.

President: Dr. Salvador Mixco Pinto.
Secretary: Dr. Daniel Alfredo Alfaro.
Treasurer: Dr. Antonio Pineda M.

SOCIEDAD ESPANOLA DE OTORRINOLARINGOLOGIA.

Presidente: Dr. D. Adolfo Hinojar Pons.
Vice-Presidente: Dr. D. Jose Perez Mateos.
Secretario General: Dr. D. Francisco Marañés.
Tesorero: Dr. D. Ernesto Alonso Ferrer.

SOCIEDAD MEXICANA DE OTORRINOLARINGOLOGIA

Monterrey 47-201
Mexico 7, D. F.

President: Dr. Rafael Giorgana.
Secretary: Dr. Carlos Valenzuela.
Treasurer: Dr. Benito Madariaga.
First Vocal: Dr. Rafael González.
Second Vocal: Dr. Juan Oberhauser.

SOCIEDAD NACIONAL DE CIRUGIA OF CUBA.

Presidente: Dr. Reinaldo de Villers.
Vice-Presidente: Dr. César Cabrera Calderin.
Secretario: Dr. José Xirau.
Tesorero: Dr. Alfredo M. Petit.
Vocal: Dr. José Gross.
Vocal: Dr. Pedro Hernández Gonzalo.

SOCIEDAD OTO-RINO-LARINGOLOGIA DE LOS HOSPITALES DE MADRID.

Presidente: Dr. Don Fernando Beltrán Castillo.
Secretario General: Dr. Don Alfonso Vassallo de Mumbert.
Tesorero: Dr. Don Rafael Garcia Tapia.

SOCIEDAD VENEZOLANA DE OTORRINOLARINGOLOGIA.

Presidente: Dr. Gabriel Briceño Romero.
Vice-Presidente: Dr. Silvestre Rincón Fuenmayor.
Secretario General: Dr. Oscar Bustamante Miranda.
Tesorero: Dr. Arturo Marrero Gómez.
Vocales: Dr. Miguel Octavio Russa, Dr. Benjamin Briceño, Dr. Oscar Gonzalez Castillo.

SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA DO RIO GRANDE DO SUL.

President: Dr. Ivo Adolpho Kuhl.
Secretary: Dr. Decio Lisboa Castro.
Treasurer: Dr. Jorge Valentin.

SOCIEDAD PANAMENA DE OTORRINOLARINGOLOGIA.

Presidente: Dr. Manuel Preciado.
First Vice-Presidente: Dr. Alonso Roy.
Second Vice-Presidente: Dr. Carlos Arango Carbone.
Secretario: Dr. Maria Esther Villalaz.
Tesorero: Dr. Ramòn Crespo.

SOCIEDADE PORTUGUESA DE OTORRINOLARINGOLOGIA E DE BRONCO-ESOFAGOLOGIA.

Presidente: Dr. Alberto Luis De Mendonca.
Vice-Presidente: Dr. Jaime de Magalhaes.
1.° Secretario: Dr. Antonio da Costa Quinta.
2.° Secretario: Dr. Albano Coelho.
Tesoureiro: Dr. Jose Antonio de Campos Henriques.
Vogais: Dr. Teofilo Esquivel.
Dr. Antonio Cancela de Amorim.
Sede: Avenida da Liberdade, 65, 1°, Lisboa.

SOCIETY OF MILITARY OTOLARYNGOLOGISTS.

President: Lt. Col. Stanley H. Bear, USAF (MC), USAF Hospital, Maxwell (Air University), Maxwell Air Force Base, Ala.
Secretary-Treasurer: Capt. Maurice Schiff, MC, USN, U. S. Naval Hospital, Oakland, Calif.
Meeting:

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. F. R. Price, 118 Rutledge Ave., Charleston, S. C.
President-Elect: Dr. L. D. Lide, 161 W. Cheves St., Florence, S. C.
Vice-President: Dr. R. E. Livingstone, 1505 Main St., Newberry, S. C.
Secretary-Treasurer: Dr. Roderick Macdonald, 330 E. Main St., Rock Hill, S. C.
Meeting: Jointly with the N. C. Society of Eye, Ear, Nose and Throat. Next joint annual meeting of The South Carolina Society of Ophthalmology and Otolaryngology and the N. C. Eye, Ear, Nose and Throat Society at Charleston, S. C., Sept. 14, 15 and 16, 1959.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY.

Chairman: Dr. V. Eugene Holcombe, Charleston, W. Va.
Chairman-Elect: Dr. G. Slaughter Fitz-Hugh, Charlottesville, Va.
Vice-Chairman: Dr. George M. Haik, New Orleans, La.
Secretary: Dr. Mercer G. Lynch, New Orleans, La.

VIRGINIA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Benjamin Sheppard, 301 Medical Arts Building, Richmond, Va.
President-Elect: Dr. Emanuel U. Wallerstein, Professional Building, Richmond, Va.
Vice-President: Dr. Calvin T. Burton, Medical Arts Building, Roanoke, Va.
Secretary-Treasurer: Dr. Maynard P. Smith, 600 Professional Building, Richmond, Va.

WEST VIRGINIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY.

President: Dr. Nime K. Joseph, Wheeling, W. Va.
President-Elect: Dr. John A. B. Holt, Charleston, W. Va.
Vice-President: Dr. William K. Marple, Huntington, W. Va.
Secretary-Treasurer: Dr. Albert C. Esposito, Huntington, W. Va.
Director for Two Years: Dr. James T. Spencer, Charleston, W. Va.
Next Meeting: Greenbrier Hotel, White Sulphur Springs, W. Va., Aug. 20-23, 1959.